

JC07 Rec'd PCT/PTO 08 JAN 2002

FORM PTO-1390 (REV 10-2000)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY'S DOCKET NUMBER 33339/242753	
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371				U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5) <b>10/030500</b> To be assigned	
INTERNATIONAL APPLICATION NO. PCT/DE00/02262		INTERNATIONAL FILING DATE July 8, 2000		PRIORITY DATE CLAIMED July 8, 1999	
TITLE OF INVENTION Vaccine Against Lentiviral Infections, Such As The Feline Immune Deficiency Virus Of The Cat					
APPLICANT(S) FOR DO/EO/US Christian Leutenegger; Mattias Schroff; Burghardt Willig; Hans Lutz					
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:					
1. <input checked="" type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a filing under 35 U.S.C. 371. 2. <input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. 371. 3. <input checked="" type="checkbox"/> This is an express request to promptly begin national examination procedures (35 U.S.C. 371(f)). 4. <input type="checkbox"/> The US has been elected by the expiration of 19 months from the priority date (PCT Article 31). 5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2)) a. <input checked="" type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau). b. <input type="checkbox"/> has been communicated by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). 6. <input checked="" type="checkbox"/> A English language translation of the International Application as filed (35 U.S.C. 371(c)(2)). 7. <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau). b. <input type="checkbox"/> have been communicated by the International Bureau. c. <input checked="" type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. d. <input type="checkbox"/> have not been made and will not be made. 8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). 9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). 10. <input type="checkbox"/> An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).					
<b>Items 11. To 16. Below concern other document(s) or information included:</b>					
11. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 C.F.R. 1.97 and 1.98. 12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. 13. <input checked="" type="checkbox"/> A FIRST preliminary amendment. <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment. 14. <input type="checkbox"/> A substitute specification. 15. <input type="checkbox"/> A change of power of attorney and/or address letter. 16. <input checked="" type="checkbox"/> Other items or information: International Preliminary Examination Report (German); Statement In Support Of Filing A Sequence Listing (Disk sent to U.S. Patent and Trademark Office, Box Sequence, P.O. Box 2327, Arlington, VA 22202 per Patent Office instructions).					

10030500-1101002  
531 Rec'd PCT/PTC 08 JAN 2002

U.S. APPLICATION NO. (If known, see 37 CFR 1.501) <b>10/030500</b> To be assigned		INTERNATIONAL APPLICATION NO. PCT/DE00/02262		ATTORNEY'S DOCKET NUMBER 33339/242753	
--	--	---	--	--	--

17. <input checked="" type="checkbox"/> The following fees are submitted:				CALCULATIONS	PTO USE ONLY
<b>Basic National Fee (37 CFR 1.492(a)(1)-(5)):</b> Neither international preliminary examination fee (37 CFR 1.482) nor International search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO				<b>\$1,040.00</b>	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO				<b>\$ 890.00</b>	<b>\$ 890.00</b>
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search (37 CFR 1.445(a)(2)) paid to USPTO				<b>\$ 740.00</b>	
International preliminary examination fee (37 CFR 1.482) paid to USPTO But all claims did not satisfy provisions of PCT Article 33(1)-(4)				<b>\$ 710.00</b>	
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4)				<b>\$ 100.00</b>	
<b>ENTER APPROPRIATE BASIC FEE AMOUNT</b>				<b>=</b>	<b>\$ 890.00</b>
Surcharge of <b>\$130.00</b> for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).				<b>\$ -0-</b>	
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total Claims	19 -20 =	0	<b>X \$18.00</b>	<b>\$ 0.00</b>	
Independent Claims	3 - 3 =	0	<b>X \$84.00</b>	<b>\$ 0.00</b>	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)				<b>+ \$280.00</b>	<b>\$</b>
<b>TOTAL OF ABOVE CALCULATIONS</b>				<b>=</b>	<b>\$ 890.00</b>
<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by one-half.				<b>\$ -0-</b>	
<b>SUBTOTAL</b>				<b>=</b>	<b>\$ 890.00</b>
Processing fee of <b>\$130.00</b> for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				<b>\$ -0-</b>	
<b>TOTAL NATIONAL FEE</b>				<b>=</b>	<b>\$ 890.00</b>
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). <b>\$40.00</b> per property				<b>+</b>	<b>\$ -0-</b>
<b>TOTAL FEES ENCLOSED</b>				<b>=</b>	<b>\$ 890.00</b>
				Amount to be	
				Refunded	\$
				Charged	\$

a. <input checked="" type="checkbox"/> A check in the amount of \$890.00 to cover the above fees is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. 16-0605 in the amount of \$ to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 16-0605.	Note: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status. SEND ALL CORRESPONDENCE TO: <div style="text-align: center; margin-top: 10px;">             SIGNATURE: Raymond O. Linker, Jr.            REGISTRATION NUMBER 26,419            ALSTON &amp; BIRD LLP            Bank of America Plaza            101 South Tryon Street, Suite 4000            Charlotte, NC 28280-4000            Tel Charlotte Office (704) 444-1000            Fax Charlotte Office (704) 444-1111  <b>Customer Number 00826</b> </div>
--	---

"Express Mail" Mailing Label Number EL 822757774 US Date of Deposit: January 8, 2002  I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to BOX PCT, Attn: DO/US (PTO) Commissioner for Patents, Washington, DC 20231. <div style="text-align: center; margin-top: 10px;">             Lorna Morehead            CLT01/4513538v1         </div>	
--	--

10030500-110102  
10/030500  
531 Rec'd PCT/F  
08 JAN 2002  
IN THE UNITED STATES DESIGNATED OFFICE (DO/US)

In re: Leutenegger, et al. Attn: DO/US  
International Appl. No.: PCT/DE00/02262  
International Filing Date: July 8, 2000  
For: Vaccine Against Lentiviral Infections,  
Such As The Feline Immune Deficiency  
Virus Of The Cat

Box PCT  
Commissioner for Patents  
Washington, DC 20231

January 8, 2002

### PRELIMINARY AMENDMENT

Sir:

Please amend the above-identified application as follows:

#### In The Claims:

1. (Amended) Vaccine for the protective vaccination or therapy of a lentivirus infection in *Felidae* comprising an immunising polynucleotide sequence which contains or consists of at least a part of the gene of a protein of the corresponding virus, particularly of the envelope protein (*env* gene), under the control of a eukaryotic promoter which is active in the corresponding animal.
2. (Amended) Vaccine in accordance with Claim 1 wherein the lentivirus is a lentivirus of an animal of the genus *Felidae*, specifically the domestic cat.
3. (Amended) Vaccine in accordance with Claim 2 wherein the lentivirus is the feline immune deficiency virus (FIV).
4. (Amended) Vaccine in accordance with Claim 1 wherein the immunising polynucleotide sequence contains a coding sequence which contains or consists of the extraviral or extracellularly situated domain of the *env* gene product, or a part of this.
5. (Amended) Vaccine in accordance with Claim 4 wherein the immunising polynucleotide sequence contains or consists of a coding sequence for at least twenty aminoacids of the transmembrane portion of the *env* gene product.

In re: Leutenegger, et al.  
Inter'l Appl. No.:PCT/DE00/02262  
Page 2 of 7

6. (Amended) Vaccine in accordance with Claim 1 which also contains at least one immunising section of the gene coding for an internal protein of the lentivirus.

7. (Amended) Vaccine in accordance with Claim 1 wherein the immunising polynucleotide sequence contains the coding sequence (SEQ ID NO. 4) of the plasmid sequence given under SEQ ID NO 1 or a sequence which is 85% identical with the coding sequence (SEQ ID NO 4) of the plasmid sequence given under SEQ ID NO 1, or a coding sequence which, without degeneration of the genetic code, is at least 85% identical with the coding sequence of the sequence given under SEQ ID NO 1.

8. (Amended) Vaccine in accordance with Claim 1 containing an accessory polynucleotide sequence which contains the sequences coding for IL-12 under the control of one or more eukaryotic promoters which are active in the corresponding animal.

9. (Amended) Vaccine in accordance with Claim 1 containing an accessory polynucleotide sequence which contains the sequence coding for IL-16 under the control of a eukaryotic promoter which is active in the corresponding animal.

10. (Amended) Vaccine in accordance with Claim 1 containing an accessory polynucleotide sequence which contains the sequence coding for IL-12 and IL-16 under the control of one or more eukaryotic promoters which are active in the corresponding animal.

11. (Amended) Vaccine in accordance with Claim 8 containing an accessory polynucleotide sequence which codes for both subunits of feline IL-12 and/or for feline IL-16 and wherein these sequences are under the control of a eukaryotic promoter which is active in the cat.

12. (Amended) Vaccine in accordance with Claim 8 containing an accessory polynucleotide sequence which contains at least one base sequence of the type  $N^1N^2CGN^3N^4$ , where  $N^1N^2$  is an element of the group GT, GG, GA, AT or AA and  $N^3N^4$  is an element of the group CT or TT.

13. (Amended) Vaccine in accordance with Claim 1 in which the immunising polynucleotide sequences and/or the accessory polynucleotide sequences are present as expression constructs which consist of linear and covalently capped molecules of desoxyribonucleic acid which contain a linear double-stranded region and in which the single strands which combine to form double strands are connected by short single-stranded loops of desoxyribonucleic acid and in which the single strands which combine to form double strands only consist of the coding sequence, a terminator sequence and a promoter which is active in the animal which is immunised.

14. (Amended) Vaccine in accordance with Claim 8 in which the accessory polynucleotide sequence contains a coding sequence in accordance with SEQ ID NO 8 (IL-12 p40), a coding sequence in accordance with SEQ ID NO 9 (IL-12 p35), coding sequences SEQ ID NO 10 (IL-16), SEQ ID NO 5 (CpG) or SEQ ID NO 6 (CpG) or a sequence which is complementary to one of these sequences.

15. (Amended) Vaccine for the vaccination or therapy of lentivirus infections in animals characterised by the presence of an immunising polynucleotide sequence and, in some cases, an accessory polynucleotide sequence in accordance with Claim 8, applied to a suitable massive and inert carrier material, in such a way that it can be accelerated into the skin of the animal, penetrate into the cells of the animal and be expressed there.

17. (Amended) Vaccine in accordance with Claim 15 which is characterised by the carrier material being gold.

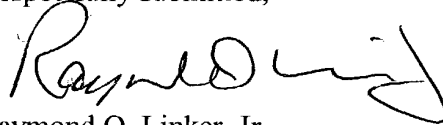
18. (Amended) Vaccine for the protective vaccination or therapy of an infection with lentivirus in *Felidae* which is characterised by the fact that it contains an immunising protein or the envelope protein of the corresponding lentivirus, together with IL-12 and/or IL-16 in the form of protein.

In re: Leutenegger, et al.  
Inter'l Appl. No.:PCT/DE00/02262  
Page 4 of 7

REMARKS

The above amendments are made to more clearly define the invention under United States practice. Please enter this amendment prior to calculation of the filing fee.

Respectfully submitted,



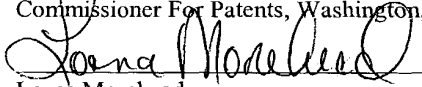
Raymond O. Linker, Jr.  
Registration No. 26,419

**ALSTON & BIRD LLP**  
Bank of America Plaza  
101 South Tryon Street, Suite 4000  
Charlotte, NC 28280-4000  
Tel Charlotte Office (704) 444-1000  
Fax Charlotte Office (704) 444-1111  
**Customer No. 00826**

**CERTIFICATE OF EXPRESS MAILING**

"Express Mail" mailing label number EL 822757774 US  
Date of Deposit January 8, 2002

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Box PCT, Commissioner For Patents, Washington, DC 20231.

  
Lorna Morehead

In re: Leutenegger, et al.  
Inter'l Appl. No.:PCT/DE00/02262  
Page 5 of 7

**Version With Markings to Show Changes Made:**

1. (Amended) Vaccine for the protective vaccination or therapy of a lentivirus infection in *Felidae* [which has the characteristic that it contains] comprising an immunising polynucleotide sequence which contains or consists of at least a part of the gene of a protein of the corresponding virus, particularly of the envelope protein (*env* gene), under the control of a eukaryotic promoter which is active in the corresponding animal.
2. (Amended) Vaccine in accordance with Claim 1 [which has the characteristic that] wherein the lentivirus is a lentivirus of an animal of the genus *Felidae*, specifically the domestic cat.
3. (Amended) Vaccine in accordance with Claim 2 [which has the characteristic that] wherein the lentivirus is the feline immune deficiency virus (FIV).
4. (Amended) Vaccine in accordance with [Claims 1 to 3 which has the characteristic that] Claim 1 wherein the immunising polynucleotide sequence contains a coding sequence which contains or consists of the extraviral or extracellularly situated domain of the *env* gene product, or a part of this.
5. (Amended) Vaccine in accordance with Claim 4 [which has the characteristic that] wherein the immunising polynucleotide sequence contains or consists of a coding sequence for at least twenty aminoacids of the transmembrane portion of the *env* gene product.
6. (Amended) Vaccine in accordance with [Claims 1 to 5 which has the characteristic that it] Claim 1 which also contains at least one immunising section of the gene coding for an internal protein of the lentivirus[, for example the *gag* gene].
7. (Amended) Vaccine in accordance with [claims 1 to 6 which has the characteristic that] Claim 1 wherein the immunising polynucleotide sequence contains the coding sequence (SEQ ID NO. 4) of the plasmid sequence given under SEQ ID NO 1 or a sequence

which is 85% identical with the coding sequence (SEQ ID NO 4) of the plasmid sequence given under SEQ ID NO 1, or a coding sequence which, without degeneration of the genetic code, is at least 85% identical with the coding sequence of the sequence given under SEQ ID NO 1.

8. (Amended) Vaccine in accordance with [Claims 1 to 7 which is characterised by] Claim 1 containing an accessory polynucleotide sequence which contains the sequences coding for IL-12 under the control of one or more eukaryotic promoters which are active in the corresponding animal.

9. (Amended) Vaccine in accordance with [Claims 1 to 7 which is characterised by] Claim 1 containing an accessory polynucleotide sequence which contains the sequence coding for IL-16 under the control of a eukaryotic promoter which is active in the corresponding animal.

10. (Amended) Vaccine in accordance with [Claims 1 to 7 which is characterised by] Claim 1 containing an accessory polynucleotide sequence which contains the sequence coding for IL-12 and IL-16 under the control of one or more eukaryotic promoters which are active in the corresponding animal.

11. (Amended) Vaccine in accordance with [Claims 8 to 10 which is characterised by] Claim 8 containing an accessory polynucleotide sequence which codes for both subunits of feline IL-12 and/or for feline IL-16 and [that] wherein these sequences are under the control of a eukaryotic promoter which is active in the cat.

12. (Amended) Vaccine in accordance with [Claims 8 to 11 which is characterised by] Claim 8 containing an accessory polynucleotide sequence which contains at least one base sequence of the type  $N^1N^2CGN^3N^4$ , where  $N^1N^2$  is an element of the group GT, GG, GA, AT or AA and  $N^3N^4$  is an element of the group CT or TT.

13. (Amended) Vaccine in accordance with [at least one of Claims 1 to 12 which is characterised by the fact that] Claim 1 in which the immunising polynucleotide sequences and/or



the accessory polynucleotide sequences are present as expression constructs which consist of linear and covalently capped molecules of desoxyribonucleic acid which contain a linear double-stranded region and in which the single strands which combine to form double strands are connected by short single-stranded loops of desoxyribonucleic acid and in which the single strands which combine to form double strands only consist of the coding sequence, a terminator sequence and a promoter which is active in the animal which is immunised.

14. (Amended) Vaccine in accordance with [Claims 8 to 13 which is characterised by the fact that] Claim 8 in which the accessory polynucleotide sequence contains a coding sequence in accordance with SEQ ID NO 8 (IL-12 p40), a coding sequence in accordance with SEQ ID NO 9 (IL-12 p35), coding sequences SEQ ID NO 10 (IL-16), SEQ ID NO 5 (CpG) or SEQ ID NO 6 (CpG) or a sequence which is complementary to one of these sequences.

15. (Amended) Vaccine [in accordance with Claims 1 to 14] for the vaccination or therapy of lentivirus infections in animals characterised by the presence of an immunising polynucleotide sequence and, in some cases, an accessory polynucleotide sequence in accordance with [Claims 8 to 12] Claim 8, applied to a suitable massive and inert carrier material, in such a way that it can be accelerated into the skin of the animal, penetrate into the cells of the animal and be expressed there.

17. (Amended) Vaccine in accordance with [Claims 15 or 16] Claim 15 which is characterised by the carrier material being gold.

18. (Amended) Vaccine for the protective vaccination or therapy of an infection with lentivirus in *Felidae* which is characterised by the fact that it contains an immunising protein or [part of a protein, particularly] the envelope protein of the corresponding lentivirus, together with IL-12 and/or IL-16 in the form of protein.

10030500 110102  
10/030500  
531 Rec'd PCT/F. 08 JAN 2002  
PATENT

Attorney's Docket No. 33339/242753

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Leutenegger, et al. Attn: DO/US  
International Appl. No.: PCT/DE00/02262  
International Filing Date: July 8, 2000  
For: Vaccine Against Lentiviral Infections,  
Such As The Feline Immune Deficiency  
Virus Of The Cat

BOX PCT  
Commissioner for Patents  
Washington, DC 20231

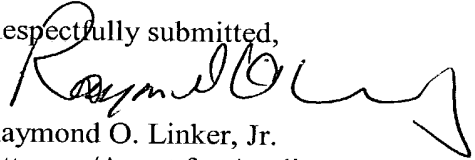
January 8, 2002

**STATEMENT IN SUPPORT OF FILING A  
SEQUENCE LISTING UNDER 37 CFR § 1.821(f)**

Sir:

I hereby state that the content of the paper and computer readable copies of the Sequence Listing, submitted concurrently herewith in accordance with 37 CFR § 1.821(c) and (e), are the same. The disk was mailed to U.S. Patent and Trademark Office, Box Sequence, P.O. Box 2327, Arlington, VA 22202, per Patent Office instructions.

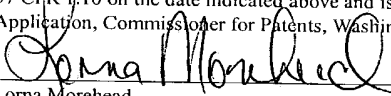
Respectfully submitted,

  
Raymond O. Linker, Jr.  
Attorney/Agent for Applicant  
Registration No. 26,419

**Customer No. 00826**  
**Alston & Bird LLP**  
Bank of America Plaza  
101 South Tryon Street, Suite 4000  
Charlotte, NC 28280-4000  
Tel Raleigh Office (919) 862-2200  
Fax Raleigh Office (919) 862-2260

"Express Mail" Mailing Label Number EL 822757774 US  
Date of Deposit: January 8, 2002

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Box Patent Application, Commissioner for Patents, Washington, DC 20231.

  
Lorna Morehead

**CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner For Patents, Washington, DC 20231, on January 8, 2002.

CLT01/4513802v1

10/030500

531 Rec'd PCT/EE 08 JAN 2002

## SEQUENCE LISTING

<110> Leutenegger, Christian  
 Schroff, Mattias  
 Willig, Burghardt  
 Lutz, Hans

<120> Vaccine Against Lentiviral Infections,  
 such as the Feline Immune Deficiency Virus of the Cat

<130> 33339/242753

<150> PCT/DE00/02262

<151> 2000-07-08

<150> CH 1258/1999

<151> 1999-07-08

<160> 10

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 5871

<212> DNA

<213> Feline lentiviruses

<220>

<221> misc\_feature

<222> (0)...(0)

<223> FIV gp140 (pMOLFIVgp140)

<400> 1

```

tcttcgcgtt cctcgcgtcac tgactcgcgtg cgctcgggtcg ttccggctgcg gcgagcggta 60
tcagctcact caaaggcggt aatacgggta tccacagaat caggggataa cgcaggaaag 120
aacatgtgag caaaaggcca gcaaaaggcc aggaaccgta aaaaggccgc gttgctggcg 180
tttttccata ggctccgccc ccctgacgag catcacaaaa atcgacgctc aagtcagagg 240
tggcgaaacc cgacaggact ataaagatac caggcgtttc cccctggaag ctccctcgtg 300
cgctctcctg ttccgaccct gccgcttacc ggatacctgt ccgcctttct cccttcggga 360
agcgtggcgc tttctcatag ctcacgctgt aggtatctca gttcgggtgta ggtcgttcgc 420
tccaagctgg gctgtgtgca cgaaccccc gttcagcccc accgctgcgc cttatccggt 480
aactatcgtc ttgagtccaa cccggtaaga cagcacttat cgccactggc agcagccact 540
ggtaacagga ttagcagagc gaggtatgta ggctgtgcta cagagttctt gaagtgggtg 600
cctaactacg gctacactag aaggacagta tttgggtatct gcgctctgct gaagccagtt 660
accttcggaa aaagagttgg tagctcttga tccggcaaac aaaccaccgc tggtagcggg 720
ggtttttttg tttgcaagca gcagattacg cgcagaaaaa aaggatctca agaagatcct 780
ttgatctttt ctacggggtc tgacgctcag tggaaacgaaa actcacgtta agggattttg 840
gtcatgagat tatcaaaaag gatcttcacc tagatccttt taaattaaaa atgaagtttt 900
aaatcaatct aaagtatata tgagtaaaact tggctgtgaca gttaccaatg cttaatcagt 960
gaggcaccta tctcagcat ctgtctatct ggctcatcca tagttgcctg actccccgtc 1020
gtgtagataa ctacgatacg ggagggctta ccatctggcc ccagtgcctg aatgataccg 1080
cgagacccac gctcaccggc tccagattta tcagcaataa accagccagc cggaagggcc 1140
gagcgagaaa gtggtcctgc aactttatcc gcctccatcc agtctattaa ttgttgccgg 1200
gaagctagag taagtagttc gccagttaat agtttgcgca acgttggtgc cattgctaca 1260

```

```

ggcatcgtgg tgtcacgctc gtcgttttgg atggcttcat tcagctccgg ttcccaacga 1320
tcaaggcgag ttacatgata ccccatgttg tgcaaaaaag cggttagctc cttegggtcct 1380
ccgatcgttg tcagaagtaa gttggccgca gtgttatcac tcatggttat ggcagcactg 1440
cataattctc ttactgtcat gccatccgta agatgctttt ctgtgactgg tgagtactca 1500
accaagtcac tctgagaata gtgtatgcgg cgaccgagtt gctcttgccc ggcgtcaata 1560
cgggataata ccgcgccaca tagcagaact ttaaaagtgc tcatcattgg aaaacgttct 1620
tcggggcgaa aactctcaag gatcttaccg ctgttgagat ccagttcgat gtaaccact 1680
cgtgcacca actgatcttc agcatctttt actttcacca gcgtttctgg gtgagcaaaa 1740
acaggaaggc aaaatgccgc aaaaaagga ataaggcgca cacggaaatg ttgaatactc 1800
atactcttcc tttttcaata ttattgaagc atttatcagg gttattgtct catgagcgga 1860
tacatatttg aatgtattta gaaaaataaa caaatagggg ttccgcgcac atttccccga 1920
aaagtgcac ctgacgtcta agaaaccatt attatcatga cattaaccta taaaaatagg 1980
cgtatcacga ggccttttcg tctcgcgcgt ttcggtgatg acggtgaaaa cctctgacac 2040
atgcagctcc cggagacggg cacagcttgt ctgtaagcgg atgccgggag cagacaagcc 2100
cgtgcggcg gtcagcggg tgttggcggt tgctggggct ggcttaacta tgcggcatca 2160
gagcagattg tactgagagt gcacatattg cgggttgaaa taccgcacag atgcgtaagg 2220
agaaaatacc gcacagggcg ccattcgcca ttcaggctgc gcaactgttg ggaagggcga 2280
tcgggtcggg cctcttcgct attacgccag ctggcgaaag ggggatgtgc tgcaaggcga 2340
ttaagttggg taacgccagg gttttccag tcacgacgtt gtaaaacgac ggccagtgcc 2400
aagcttgcca attctggatc cgctagctta accgtattac cgccatgcat tagttattaa 2460
tagtaatcaa ttacggggtc attagttcat agcccatata tggagttccg cgttacataa 2520
cttacggtaa atggcccgc tggtgaccg ccaacgacc cccgccatt gacgtcaata 2580
atgacgtatg ttcccatagt aacgccaaat gggactttcc attgacgtca atgggtggag 2640
tatttacggt aaactgccca cttggcagta catcaagtgt atcatatgcc aagtacgccc 2700
cctattgacg tcaatgacgg taaatggccc gcctggcatt atgccagta catgacctta 2760
tgggactttc ctacttgcca gtacatctac gtattagtca tcgctattac catggtgatg 2820
cggttttggc agtacatcaa tgggcgtgga tagcggtttg actcacgggg atttccaagt 2880
ctccacccca ttgacgtcaa tgggagtttg ttttggcacc aaaatcaacg ggactttcca 2940
aaatgtcgta acaactccgc ccattgacg caaatggcg gttaggcgtgt acggtgggag 3000
gtctatataa gcagagctgg tttagtgaag cgtcagatgg taccatggca gaaggattg 3060
cagccaatag acaatggata gggccagaag aagctgaagg gttgttagat tttgatataa 3120
caacacaaat gaatgaagaa gggccactaa atccaggaat aaacccattt aggggtgcctg 3180
gaatagcaga aatagaaaag cgagactatt gcaaaatatt acaacccaaa ttacaagatc 3240
taaagaatga aattcaagag gtaaaactgg aagaaggaaa tgcaggtaag tttagaagag 3300
caagattttt aagatattct gatgaaaata tattatccct gattcatttg ttcatagggg 3360
attgtacata tttatgcaga aaaaatgagt taggatcttt acgacatgac atagatatag 3420
acgaactaca agaagatga tatactagta tagagaaagg tacaactgcc aatataaaa 3480
atggtagacg atgtctcata ggaacagcgg ctttgtacct gcttttcata ggaataataa 3540
tatatacaca aacaaccaag gctcaggtag tatggagact tccaccatta gtagtccccg 3600
tgaaagaatc agagataatt ttttgggatt gttgggcacc agaggaaccc gcctgtcagg 3660
actttcttgg ggcaatgata catctaaaag ctagtacaaa tataagtata caagagggac 3720
ctaccctggg gaattgggct agagaaatat ggggaacatt attcaaaaag gctaccagac 3780
aatgtagaag aggtagagta tggagaagat ggaatgagac tataacagga ccatcaggat 3840
gtgctaataa cacatgttat aatatctcag taatagtacc tgattatcaa tgttatttag 3900
acagagtaga tacttgggta caagggaag taaatatatc attatgtcta acaggaggaa 3960
aaatgttgta taataaatat acaaaacaat tgagctattg tacagatcca ttacaaatcc 4020
cactgatcaa ttatacgttt ggacctaatc aaacatgtaa gtggaacact tcacagattc 4080
aagactctga gataccaaaa tgtggatggg ggaatcaagc agcctattat aacagttgta 4140
gatgggaaag cactgatgta aagtttcatt gtcaaagaac acagagtctg cctggaacat 4200
ggcttagaac aatctcatca tggaggccaa agaatagatg ggaatggagg ccagattttg 4260
aaagtgaaaa agtgaaaagta tctctacagt gtaatagcac aagcaaccta accttgcaa 4320
tgagaagttc aggagattat ggagaggtaa cgggagcatg gatagaattt ggatgtcata 4380
ggaaaaaatc aaaacttcac tctggaagaa ggtttagaat cagatgtaga tgggataaag 4440
gggataatac ctcactcatt gatacatgtg gaaaaactca aaatgtttta ggtgcaaatc 4500
ctgtagattg caccatgtat gcaaatagaa tgtataattg ttctttacaa aatgggttta 4560
ctatgaagat agatgacctt gttatgcatt tcaatatgac gaaagctgta gaaatgtata 4620
acattgctgg aaattggtct tgtacatctg acttgccacc aacatggggg tatatgaatt 4680

```

```

gtaattgtac aaatagtagt agtacaacta gtagttctgg taataaaatg gcatgtcctg 4740
gagataaagg tatcttaaga aattgggtata acccagtagc aggattaaga caatccctag 4800
aaaagtatca agtagtaaaa caaccagatt acttagtggt gccaggggaa gtcattggaat 4860
ataaacctag aaggaaaaga gcagctattc atgttatgtt agctcttgca acagtattat 4920
ctatggccgg ggcagggacg ggggctactg ctatagggat ggtaacgcaa taccaccaag 4980
ttctggcaac tcatcaagaa gctatagaaa aggtgactga agccttaaag ataaacaact 5040
taagattagt tacattagag catcaagtac tagtaatagg attaaaagta gaagctatgg 5100
aaaaattttt atatacagct ttcgctatgc aagaattagg atgtaatcaa aatcaattct 5160
tctgtaaagt cctcctgtg ttgtgggaaa gatataatat gactataaat caaacaatat 5220
ggaatcatgg aaatataact ttgggggaat ggtataacca aacaaaagat ttacaacaaa 5280
agttctatga aataataatg gacatagaac aaaataatgt acaaggaaaa aaagggttac 5340
aacaattaca aaaatgggaa gattgggtag gatggatagg aaatattcca aaatatttat 5400
aagagctcat aatcagccat accacatttg tagaggtttt acttgcttta aaaacctcc 5460
cacacctccc cctgaacctg aaacataaaa tgaatgcaat tcttggtggt aacttggtta 5520
ttgcagctta taatggttac aaataaagca atagcatcac aaatttcaca aataaagcat 5580
ttttttcact gcattctagt tgtggtttgt ccaactcat caatgtatct taacgcgaat 5640
tcgtaatcat ggtcatagct gtttcctgtg tgaaattggt atccgctcac aattccacac 5700
aacatacgag ccggaagcat aaagtgtaaa gcctgggggtg cctaattgagt gagctaactc 5760
acattaattg cgttgcgctc actgcccgtt ttccagtcgg gaaacctgtc gtgccagctg 5820
cattaatgaa tcggccaacg cgcggggaga ggcggtttgc gtattgggcg c 5871

```

```

<210> 2
<211> 4522
<212> DNA
<213> Felis catus

```

```

<220>
<221> misc_feature
<222> (0)...(0)
<223> IL-12p40

```

```

<400> 2
tcttccgctt cctcgctcac tgactcgctg cgctcggtcg ttccggctgcg gcgagcggtta 60
tcagctcact caaaggcggg aatacgggta tccacagaat caggggataa cgcaggaaaag 120
aacatgtgag caaaaggcca gcaaaaggcc aggaaccgta aaaaggccgc gttgctggcg 180
tttttccata ggctccgccc ccctgacgag catcacaaaa atcgacgctc aagtcagagg 240
tggcgaaacc cgacaggact ataaagatac caggcggttc cccctggaag ctccctcggtg 300
cgctctcctg ttccgaccct gccgcttacc ggatacctgt ccgcctttct cccttcggga 360
agcgtggcgc tttctcatag ctacgctgtt aggtatctca gttcggtgta ggtcggtcgc 420
tccaagctgg gctgtgtgca cgaacccccg gttcagcccc accgctgcgc cttatccggt 480
aactatcgtc ttgagtccaa cccggttaaga cagcacttat cgccactggc agcagccact 540
ggtaacagga ttagcagagc gaggtatgta ggcggtgcta cagagttctt gaagtgggtg 600
cctaactacg gctacactag aaggacagta tttggtatct gcgctctgct gaagccagtt 660
accttcggaa aaagagttgg tagctcttga tccggcaaac aaaccaccgc tggtagcggt 720
ggtttttttg tttgcaagca gcagattacg cgcagaaaaa aaggatctca agaagatcct 780
ttgatctttt ctacgggggtc tgacgctcag tggaaacgaaa actcacgtta agggattttg 840
gtcatgagat tatcaaaaag gatcttcacc tagatccttt taaattaaaa atgaagtttt 900
aatcaatct aaagtatata tgagtaaaat tggcttgaca gttaccaatg cttaatcagt 960
gaggcaccta tctcagcgat ctgtctattt cggtcatcca tagttgcctg actccccgtc 1020
gtgtagataa ctacgatacg ggaggggctta ccatctggcc ccagtgtgctc aatgataccg 1080
cgagaccac gctcaccggc tccagattta tcagcaataa accagccagc cggaaggggc 1140
gagcgagaa gtggctcctgc aactttatcc gcctccatcc agtctattaa ttgttgccgg 1200
gaagctagag taagtagttc gccagttaat agtttgcgca acgttggtgc cattgctaca 1260
ggcatcggtg tgctacgctc gtcgttttgt atggcttcat tcagctccgg ttcccaacga 1320
tcaaggcgag ttacatgatc ccccatgttg tgcaaaaaag cgggttagctc cttcggtcct 1380

```

```

ccgategttg tcagaagtaa gttggccgca gtgttatcac tcatggttat ggcagcactg 1440
cataattctc ttactgtcat gccatccgta agatgctttt ctgtgactgg tgagtactca 1500
accaagtcac tctgagaata gtgtatgcgg cgaccgagtt gctcttgccc ggcgtcaata 1560
cgggataata ccgcgccaca tagcagaact ttaaaagtgc tcatcattgg aaaacgttct 1620
tcggggcgaa aactctcaag gatcttaccg ctggtgagat ccagttcgat gtaaccact 1680
cgtgcaccca actgatcttc agcatctttt actttcacca gcgtttctgg gtgagcaaaa 1740
acaggaaggc aaaatgccgc aaaaaaggga ataaggcgca cacggaaatg ttgaatactc 1800
atactcttcc tttttcaata ttattgaagc atttatcagg gttattgtct catgagcgga 1860
tacatatttg aatgtattta gaaaaataaa caaatagggg ttccgcgcac atttccccga 1920
aaagtgcac ctgacgtcta agaaaccatt attatcatga cattaaccta taaaaatagg 1980
cgtatcacga ggccttttcg tctcgcgcgt ttcgggtgat acggtgaaaa cctctgacac 2040
atgcagctcc cggagacggg cacagcttgt ctgtaagcgg atgccgggag cagacaagcc 2100
cgtcagggcg cgtcagcggg tgttggcggg tgtcggggct ggcttaacta tgcggcatca 2160
gagcagattg tactgagagt gcaccatatt cgggtgtgaaa taccgcacag atgcgtaagg 2220
agaaaatacc gcacagggcg ccattcgcca ttcaggctgc gcaactgttg ggaaggcgga 2280
tcgggtcggg cctcttcgct attacgccag ctggcgaaaag ggggatgtgc tgcaaggcga 2340
ttaagttggg taacgccagg gttttccag tcacgacgtt gtaaaacgac ggccagtgcc 2400
aagcttggtc tccccctgga tccgctagct taaccgtatt accgccatgc attagttatt 2460
aatagtaate aattacgggg tcattagttc atagcccata tatggagttc cgcgttacat 2520
aacttacggt aatggcccg cctggtgac cgcccaacga cccccgcca ttgacgtcaa 2580
taatgacgta tgttcccata gtaacgcaa tagggacttt ccattgacgt caatgggtgg 2640
agtatttacg gtaaacgtgc cacttggcag tacatcaagt gtatcatatg ccaagtacgc 2700
ccctatttga cgtcaatgac ggtaaatggc ccgcctggca ttatgccag tacatgacct 2760
tatgggactt tctacttg cagtacatct acgtattagt catcgctatt accatggtga 2820
tgcggttttg gcagtacatc aatgggcgtg gatagcgggt tgactcacgg ggatttccaa 2880
gtctccacc cattgacgtc aatgggagtt tgttttgga ccaaaatcaa cgggactttc 2940
caaaatgtcg taacaactcc gcccattga cgcaaatggg cggtaggcgt gtacggtggg 3000
aggtctatat aagcagagct ggtttagtga accgtcagat ggtaccatgc atcctcagca 3060
gttggtcate gcttggtttt ccttggtttt gctggcacct cccctcatgg ccatatggga 3120
actggagaaa aacgtttatg ttgtagagtt ggactggcac cctgatgccc ccggagaaat 3180
ggtggtcctt acctgcaata ctctgaaga agatgacatc acctggacct ctgaccagag 3240
cagtgaagtc ctaggctctg gtaaaactct gaccatccaa gtcaaagaat ttgcagatgc 3300
tggccagtat acctgtcata aaggaggcga ggttctgagc cattcgttcc tcctgataca 3360
caaaaaggaa gatggaattt ggtccactga tatcttaagg gaacagaaag aatccaaaaa 3420
taagatcttt ctaaaatgtg aggcгааааа ttattctgga cgtttcacct gctggtggct 3480
gacggcaatc agtaccgatt tgaaattcac tgtcaaaagc agcagaggct cctctgacct 3540
ccaaggggtg acttgtggag cagcgacact ctacgacag aaggtcagag tggacaacag 3600
ggattataag aagtacacag tggagtgtca ggagggcagt gcctgcccgg ctgccgagga 3660
gagcctaccc attgaagtcg tggtgacgc tattcacaag ctcaagtacg aaaactacac 3720
cagcagcttc ttcacaggg acatcatcaa accggaccca cccaagaacc tgcaactgaa 3780
gccattaaaa aattctcggc atgtggaagt gagctgggaa taccctgaca cctggagcac 3840
cccacattcc tacttctcct taacatttgg cgtacaggtc cagggcaaga acaacagaga 3900
aaagaaagac agactctccg tggacaagac ctacagccaag gtcgtgtgcc acaaggatgc 3960
caagatccgc gtgcaagcca gggaccgcta ctatagctca tcctggagca actgggcatc 4020
cgtgtcctgc agttaggagc tcataatcag ccataaccaca tttgtagagg ttttacttgc 4080
tttaaaaaac ctcccacacc tccccctgaa cctgaaacat aaaatgaatg caattcttgt 4140
tgttaaactg tttattgcag cttataatgg ttacaaataa agcaatagca tcacaaattt 4200
cacaaataaa gcattttttt cactgcattc tagttgtggg ttgtccaaac tcatcaatgt 4260
atcttaacgc gaattcaggg ggagacccaa ttcgtaatca tggtcatagc tgtttctgt 4320
gtgaaattgt tatccgctca caattccaca caacatacga gccggaagca taaagtgtaa 4380
agcctggggg gcctaattgag tgagctaact cacattaatt gcgttgcgct cactgcccgc 4440
ttccagtcg ggaaacctgt cgtgccagct gcattaatga atcggccaac gcgcggggag 4500
aggcggtttg cgtattgggc gc 4522

```

```

<210> 3
<211> 4201
<212> DNA

```

<213> Felis catus

<220>

<221> misc\_feature

<222> (0)...(0)

<223> IL-12p35 (pMOLfIL-12p35 (e-,\_e31-) clone 61)

<400> 3

```

tcttcgcgtt cctcgcctcac tgactcgcgtg cgctcggctcg ttcggctgctg gcgagcggta 60
tcagctcact caaaggcggg aatacgggta tccacagaat caggggataa cgcaggaaag 120
aacatgtgag caaaaggcca gcaaaaggcc aggaaccgta aaaaggccgc gttgctggcg 180
tttttccata ggctccgccc ccctgacgag catcacaaaa atcgacgctc aagtcagagg 240
tggcgaaacc cgacaggact ataaagatac caggcggtttc cccctggaag ctccctcggtg 300
cgctctcctg ttccgaccct gccgcttacc ggatacctgt ccgcctttct cccttcggga 360
agcgtggcgc tttctcatag ctacgcgtgt aggtatctca gttcgggtgta ggtcggtcgc 420
tccaagctgg gctgtgtgca cgaaccccc gttcagcccg accgctgcgc cttatccggg 480
aactatcgct ttgagtccaa cccggtaaga cagacttat cgccactggc agcagccact 540
ggtaacagga ttagcagagc gaggtatgta ggcgggtgta cagagttctt gaagtgggtg 600
cctaactacg gctacactag aaggacagta tttgggtatct gcgctctgct gaagccagtt 660
accttcggaa aaagagttgg tagctcttga tccggcaaac aaaccaccgc tggtagcggg 720
ggtttttttg tttgcaagca gcagattacg cgcagaaaaa aaggatctca agaagatcct 780
ttgatctttt ctacggggtc tgacgctcag tggaaacgaa actcacgtta agggattttg 840
gtcatgagat tatcaaaaag gatcttcacc tagatccttt taaattaaaa atgaagtttt 900
aaatcaatct aaagtatata tgagtaaact tgggtctgaca gttaccaatg cttaatcagt 960
gaggcaccta tctcagcgat ctgtctattt cgttcatcca tagttgctg actccccgtc 1020
gtgtagataa ctacgatacg ggagggctta ccactctggc ccagtgcctg aatgataccg 1080
cgagacccac gctcaccggc tccagattta tcagcaataa accagccagc cggaagggcc 1140
gagcgcagaa gtggtcctgc aactttatcc gcctccatcc agtctattaa ttggtgccgg 1200
gaagctagag taagtagttc gccagttaat agtttgcgca acggtgttgc cattgtctca 1260
ggcatcgtgg tgtcacgctc gtctgttggt atggcttcat tcagctccgg ttcccaacca 1320
tcaaggcgag ttacatgac ccccatgttg tgcaaaaaag cggttagctc cttcggctct 1380
ccgatcgttg tcagaagtaa gttggccgca gtgttatcac tcatggttat ggcagcactg 1440
cataattctc ttactgtcat gccatccgta agatgctttt ctgtgactgg tgagtactca 1500
accaagtcac tctgagaata gtgtatgcgg cgaccgagtt gctcttgccc ggcgtcaata 1560
cgggataata ccgcgccaca tagcagaact ttaaaagtgc tcatcattgg aaaacgttct 1620
tcggggcgaa aactctcaag gatcttaccg ctggtgagat ccagttcgat gtaaccact 1680
cgtgcaccca actgatcttc agcatctttt actttacca gcgtttctgg gtgagcaaaa 1740
acaggaaggc aaaatgccgc aaaaaaggga ataaggcgca cacggaaatg ttgaatactc 1800
atactcttcc tttttcaata ttattgaagc atttatcagg gttattgtct catgagcgga 1860
tacatatttg aatgtattta gaaaaataaa caaatagggg ttccgcgcac atttccccga 1920
aaagtgccac ctgacgtcta agaaaccatt attatcatga cattaacct taaaaatagg 1980
cgtatcacga ggccctttcg tctcgcgcgt ttcgggtgat acggtgaaaa cctctgacac 2040
atgcagctcc cggagacggg cacagcttgt ctgtaagcgg atgccgggag cagacaagcc 2100
cgtcagggcg cgtcagcggg tgttggcggg tgtcggggct ggcttaacta tgcggcatca 2160
gagcagattg tactgagagt gcaccatagt cgggtgtaaa taccgcacag atgcgtaagg 2220
agaaaatacc gcatcaggcg ccattcgcca ttcaggctgc gcaactgttg ggaaggcgga 2280
tcgggtgcgg cctcttcgct attacgccag ctggcgaaag ggggatgtgc tgcaaggcga 2340
ttaagttggg taacgccagg gttttccag tcacgacgtt gtaaaacgac ggccagtgcc 2400
aagcttgggt tccccctgga tccgctagct taaccgtatt accgccatgc attagttatt 2460
aatagtaate aattacgggg tcattagttc atagcccata tatggagttc cgcgttacat 2520
aacttacggt aaatggccc cctggtgcac cgcccaacga cccccgcca ttgacgtcaa 2580
taatgacgta tgttccata gtaacgcaa tagggacttt ccattgacgt caatgggtgg 2640
agtattttac gtaaaactgc cacttggcag tacatcaagt gtatcatatg ccaagtacat 2700
cccctattga cgtcaatgac ggtaaatggc ccgcttgcca ttatgccag tacatgacct 2760
tatgggactt tctacttgg cagtacatct acgtattagt catcgctatt accatggtga 2820
tgcggttttg gcagtacatc aatgggcgtg gatagcgggt tgactcacgg ggatttccaa 2880
gtctccaccc cattgacgtc aatgggagtt tgttttggca ccaaaatcaa cgggactttc 2940

```

```

caaaatgtcg taacaactcc gccccattga cgcaaatggg cggtaggcgt gtacgggtggg 3000
aggtctatat aagcagagct ggtttagtga accgtcagat ggtaccatgt gcccgcgcgc 3060
tggcctcctc cttgtaacca tcctggctct gttaaaccac ctggaccacc tcagtttggc 3120
caggaacctc cccacaccca caccaagccc aggaatgttc cagtgcctca accactccca 3180
aaccctgctg cgagccatca gcaacacgct tcagaaggcc agacaaactc tagaatttta 3240
cccctgcact tccgaagaga ttgatcatga agatatcaca aaagataaaa ccagcacagt 3300
ggaggcctgc ttaccactgg aattagccat gaatgagagt tgcttggctt ccagagagat 3360
ctctctgata actaatggga gttgcctggt gtccagaaag acctctttta tgacgacct 3420
gtgccttagc agtatctatg aggacttgaa gatgtaccag gtggagtcca aggccatgaa 3480
tgcaaagctg ttaatggatc ctaaaaggca gatctttctg gatcaaaaca tgctgacagc 3540
tattgatgag ctgatgcagg ccctgaattt caacagtgtg actgtgccac agaactcctc 3600
ccttgaagaa ccggattttt ataaaactaa aatcaagctc tgcatacttc ttcatgcttt 3660
cagaatccgt gcagtgacca tcaatagaat gatgagctat ctgaatgctt cctaggagct 3720
cataatcagc cataccacat ttgtagaggt tttacttgct ttaaaaaacc tcccacacct 3780
ccccctgaac ctgaaacata aaatgaatgc aattgttggt gttaacttgt ttattgcagc 3840
ttataatggt tacaataaaa gcaatagcat cacaaatttc acaaataaag catttttttc 3900
actgcattct agttgtggtt tgtccaaact catcaatgta tcttaacgcg aattcagggg 3960
gagacccaat tcgtaatcat ggatcatagc gtttcctgtg tgaaatttgt atccgctcac 4020
aattccacac aacatacgag ccggaagcat aaagtgtaaa gcctgggggtg cctaatgagt 4080
gagctaactc acattaattg cgttgcgctc actgcccgct ttccagtcgg gaaacctgtc 4140
gtgccagctg cattaatgaa tcggccaacg cgcggggaga ggcggtttgc gtattgggcy 4200
c

```

4201

```

<210> 4
<211> 3903
<212> DNA
<213> Felis catus

```

```

<220>
<221> misc_feature
<222> (0)...(0)
<223> IL-16

```

```

<400> 4
tcttcgcgtt cctcgctcac tgactcgctg cgctcggtcg ttccggctgcg gcgagcggta 60
tcagctcact caaaggcggg aatacgggta tccacagaat caggggataa cgcaggaaag 120
aacatgtgag caaaaggcca gcaaaaggcc aggaaccgta aaaaggccgc gttgctggcg 180
tttttccata ggctccgccc ccctgacgag catcacaaaa atcgacgctc aagtcagagg 240
tggcgaaaacc cgacaggact ataaagatac caggcggttc ccctggaag ctccctcgctg 300
cgctctcctg ttccgacctt gccgcttacc ggatacctgt ccgcctttct cccttcggga 360
agcgtggcgc tttctcatag ctacgctgtt aggtatctca gttcgggtgta ggtcgttcgc 420
tccaagctgg gctgtgtgca cgaaccccc gttcagcccc accgctgcgc cttatccggg 480
aactatcgct ttgagtccaa cccggttaaga cacgacttat cgccactggc agcagccact 540
ggtaacagga ttagcagagc gaggtatgta ggcgggtgcta cagagttcct gaagtgggtg 600
cctaactacg gctacactag aaggacagta tttgggtatct gcgctctgct gaagccagtt 660
accttcggaa aaagagttgg tagctcttga tccggcaaac aaaccaccgc tggtagcggg 720
gggttttttg tttgcaagca gcagattacg cgcagaaaaa aaggatctca agaagatcct 780
ttgatctttt ctacggggtc tgacgctcag tggaaacgaaa actcacgtta agggattttg 840
gtcatgagat tatcaaaaag gatcttcacc tagatccttt taaattaaaa atgaagtttt 900
aaatcaatct aaagtatata tgagtaaact tgggtctgaca gttaccaatg cttaatcagt 960
gaggcaccta tctcagcgat ctgtctatct cgttcatcca tagttgcctg actccccgtc 1020
gtgtagataa ctacgatacg ggagggttta ccactctggcc ccagtgtctg aatgataaccg 1080
cgagacccac gctcaccggc tccagattta tcagcaataa accagccagc cggaagggcc 1140
gagcgcagaa gtggtcctgc aactttatcc gctccatcc agtctattaa ttgttgccgg 1200
gaagctagag taagtagttc gccagttaat agtttgcgca acgttggtgc cattgtctaca 1260
ggcatcgtag tgtcacgctc gtcgtttggg atggcttcat tcagctccgg ttcccaacga 1320
tcaaggcgag ttacatgatc ccccatgttg tgcaaaaaag cggttagctc cttcggctct 1380

```



```

ccgatcggtg tcagaagtaa gttggccgca gtgttatcac tcatggttat ggcagcactg 1440
cataattctc ttactgtcat gccatccgta agatgctttt ctgtgactgg tgagtactca 1500
accaagtcac tctgagaata gtgtatgcgg cgaccgagtt gctcttgccc ggcgtcaata 1560
cgggataata ccgcgccaca tagcagaact ttaaaagtgc tcatcattgg aaaacgttct 1620
tcggggcgaa aactctcaag gatcttaccg ctggtgagat ccagttcgat gtaaccact 1680
cgtgcaccca actgatcttc agcatctttt actttcacca gcgtttctgg gtgagcaaaa 1740
acaggaaggc aaaatgccgc aaaaaaggga ataaggcgca cacggaatg ttgaatactc 1800
atactcttcc tttttcaata ttattgaagc atttatcagg gttattgtct catgagcgga 1860
tacatatttg aatgtattta gaaaaataaa caaatagggg ttccgcgcac atttccccga 1920
aaagtgccac ctgacgtcta agaaaccatt attatcatga cattaaccta taaaaatagg 1980
cgtatcacga ggccctttcg tctcgcgcgt ttcggtgatg acggtgaaaa cctctgacac 2040
atgcagctcc cggagacggg cacagcttgt ctgtaagcgg atgccgggag cagacaagcc 2100
cgtcagggcg cgtcagcggg tgttggcggg tgctggggct ggcttaacta tgcggcatca 2160
gagcagattg tactgagagt gcaccatatt cgggtgtgaa taccgcacag atgcgtaagg 2220
agaaaatacc gcatcaggcg ccattcgcca ttcaggctgc gcaactgttg ggaaggcgga 2280
tcgggtgcgg cctcttcgct attacgccag ctggcgaaag ggggatgtgc tgcaaggcga 2340
ttaagttggg taacgccagg gttttcccg tcacgacgtt gtaaaacgac ggccagtgcc 2400
aagcttgcca attctggatc cgctagctta accgtattac cgccatgcat tagttattaa 2460
tagtaatcaa ttacggggtc attagttcat agcccatata tggagttccg cgttacataa 2520
cttacggtaa atggcccgc tggctgaccg cccaacgacc cccgccatt gacgtcaata 2580
atgacgtatg ttcccatagt aacgccaata gggactttcc attgacgtca atgggtggag 2640
tatttacggt aaactgccca cttggcagta ttcaggctgt atcatatgcc aagtacgccc 2700
cctattgacg tcaatgacgg taaatggccc gcctggcatt atgccagta catgacctta 2760
tgggactttc ctacttgcca gtacatctac gtattagtca tcgctattac catggtgatg 2820
cggttttggc agtacatcaa tgggcgtgga tagcggtttg actcacgggg atttccaagt 2880
ctccacccca ttgacgtcaa tgggagtttg ttttggcacc aaaatcaacg ggactttcca 2940
aaatgtcgta acaactccgc cccattgacg caaatggcg gtaggcgtgt acggtgggag 3000
gtctatataa gcagagctgg tttagtgaac cgtcagatgg taccatgccc gacctcaact 3060
cctccactga ttctacaaac tcggcttctg tggccagcga cgtttctggg gattccacgg 3120
aggccacggt gcacacgggt acgctggaga agacgtccgc ggggctgggc ttcagcctgg 3180
aaggcggcaa gggctccctg ctcggggaca agcctctcac cgtgaacagg attttcaaag 3240
gggcagcctc ggaacagagc gagacgatcc agccgggaga tgaaatctta cacttggccg 3300
gcactgccgt gcaggggctc acgcggtttg aagcctggaa cgttatcaag acgttgccctg 3360
acggccccgt cacgatcgtc atcaggagga gaagcgtcca gtcctcgga accacagctg 3420
ctggagactc ctaggagctc ataatcagcc ataccacatt thtagagggt ttacttgctt 3480
taaaaaacct cccacacctc cccctgaacc tgaaacataa aatgaatgca attcttgttg 3540
ttaattgtt tataatggtt acaaataaag caatagcatc acaaatttca 3600
caaataaagc atttttttca ctgcattcta gttgtggttt gtccaaactc atcaatgtat 3660
cttaacgcga attcgtaatc atggtcatag ctgtttcctg tgtgaaattg ttatccgctc 3720
acaattccac acaacatacg agccggaagc ataaagtgtg aagcctgggg tgcctaataga 3780
gtgagctaac tcacattaat tgcgttgcgc tcaactgccc ctttccagtc gggaaacctg 3840
tcgtgccagc tgcattaatg aatcgccaa cgcgcgggga gaggcggttt gcgtattggg 3900
cgc 3903

```

```

<210> 5
<211> 33
<212> DNA
<213> Artificial Sequence

```

```

<220>
<223> Oligonucleotide

```

```

<221> misc_feature
<222> (0)...(0)
<223> CpG

```

```

<400> 5

```

gttcttcggg gcgttctttt ttaagaacgc ccc

33

<210> 6  
 <211> 35  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Oligonucleotide

<221> misc\_feature  
 <222> (0)...(0)  
 <223> CpG

<400> 6  
 gaagaacggtt ttccaatgat ttttcattgg aaaac

35

<210> 7  
 <211> 2358  
 <212> DNA  
 <213> Feline lentiviruses

<220>  
 <221> misc\_feature  
 <222> (0)...(0)  
 <223> Coding Sequence for SEQ ID NO:1, FIV env Gen

<400> 7  
 atggcagaag gatttgcagc caatagacaa tggatagggc cagaagaagc tgaaggggtg 60  
 ttagattttg atatagcaac acaaatgaat gaagaagggc cactaaatcc aggaataaac 120  
 ccatttaggg tgcctggaat agcagaaaata gaaaagcgag actattgcaa aatattacaa 180  
 cccaaattac aagatctaaa gaatgaaatt caagaggtaa aactggaaga aggaaatgca 240  
 ggtaagttta gaagagcaag atttttaaga tattctgatg aaaatatatt atccctgatt 300  
 catttgttca taggggtattg tacatatatta tgcagaaaaa atgagttagg atctttacga 360  
 catgacatag atatagacga acatcaagaa gagtattata ctagtataga gaaaggtaca 420  
 actgccaaata taaaatatgg tagacgatgt ctcataggaa cagcggcttt gtacctgctt 480  
 ttcataggaa taataatata tacacaaaaca accaaggctc aggtagtatt gagacttcca 540  
 ccattagttag tccccgtgaa agaatacagag ataatttttt gggattgttg ggcaccagag 600  
 gaacccgcct gtcaggactt tcttggggca atgatacatc taaaagctag tacaaatata 660  
 agtatacaag agggacctac cctgggggaat tgggctagag aaatatgggg aacattattc 720  
 aaaaaggcta ccagacaatg tagaagaggt agagtatgga gaagatggaa tgagactata 780  
 acaggaccat caggatgtgc taataacaca tggtataata tctcagtaat agtacctgat 840  
 tatcaatggt atttagacag agtagatact tgggtacaag ggaaagtaaa tatatcatta 900  
 tgtctaacag gaggaaaaat gttgtataat aaatatacaa aacaattgag ctattgtaca 960  
 gatccattac aaatcccact gatcaattat acgtttggac ctaatcaaac atgtaagtgg 1020  
 aacacttcac agattcaaga ctctgagata ccaaaatgtg gatggtggaa tcaagcagcc 1080  
 tattataaca gttgtagatg ggaaagcact gatgtaaagt ttcattgtca aagaacacag 1140  
 agtctgcctg gaacatggct tagaacaatc tcatcatgga ggccaaagaa tagatgggaa 1200  
 tggaggccag attttgaaag tgaaaaagtg aaagtatctc tacagtgtaa tagcacaagc 1260  
 aacctaacct ttgcaatgag aagttcagga gattatggag aggtaacggg agcatggata 1320  
 gaatttggat gtcataggaa aaaatcaaaa ctctattctg aagcaagggt tagaatcaga 1380  
 tgtagatggg ataaaagggga taataacctca ctcatgtata catgtggaaa aactcaaaat 1440  
 gtttttaggtg caaatcctgt agattgcacc atgtatgcaa atagaatgta taattgttcc 1500  
 ttacaaaatg ggtttactat gaagatagat gacctgtgta tgcatttcaa tatgacgaaa 1560  
 gctgtagaaa tgtataacat tgctggaaat tggctctgta catctgactt gccaccaaca 1620  
 tgggggtata tgaattgtaa ttgtacaaat agtagtagta caactagtag ttctggtaat 1680  
 aaaatggcat gtcctggaga taaaggtatc ttaagaaatt ggtataaccc agtagcagga 1740

```

ttaagacaat ccctagaaaa gtatcaagta gtaaaacaac cagattactt agtgggtgcca 1800
ggggaagtca tggaatataa acctagaagg aaaagagcag ctattcatgt tatgttagct 1860
cttgcaacag tattatctat ggccggggca gggacggggg ctactgctat agggatggta 1920
acgcaatatc accaagttct ggcaactcat caagaagcta tagaaaaggt gactgaagcc 1980
ttaagataa acaacttaag attagttaca ttagagcatc aagtactagt aataggatta 2040
aaagtagaag ctatggaaaa atttttatat acagctttcg ctatgcaaga attaggatgt 2100
aatcaaaatc aattcttctg taaagtccct cctgtgttgt gggaaagata taatatgact 2160
ataaatcaaa caatatggaa tcatggaaat ataactttgg gggaatggta taaccaaaca 2220
aaagatttac aacaaaagtt ctatgaaata ataatggaca tagaacaaaa taatgtacaa 2280
ggaaaaaaag gggtacaaca attacaaaaa tgggaagatt gggtaggatg gataggaaat 2340
attccaaaat atttataa                                     2358

```

<210> 8

<211> 990

<212> DNA

<213> Felis catus

<220>

<221> misc\_feature

<222> (0)...(0)

<223> Coding Sequence for SEQ ID NO:2, IL-12p40

<400> 8

```

atgcacctc agcagttggt catcgctgg tttccctgg ttttgctggc acctccctc 60
atggccatat ggggaactgga gaaaaacgtt tatgtttag agttggactg gcaccctgat 120
gcccccgag aaatggtggt ccttacctgc aatactcctg aagaagatga catcacctgg 180
acctctgacc agagcagtga agtcctaggc tctggtaaaa ctctgaccat ccaagtcaaa 240
gaatttgcat atgctggcca gtatacctgt cataaaggag gcgaggttct gagccattcg 300
ttcctcctga tacacaaaaa ggaagatgga atttgggtcca ctgatattct aagggacacag 360
aaagaatcca aaaataagat ctttctaaaa tgtgaggcaa agaattattc tggacgtttc 420
acctgctggc ggctgacggc aatcagtacc gatttgaaat tcactgtcaa aagcagcaga 480
ggctcctctg acccccaagg ggtgacttgt ggagcagcga cactctcagc agagaaggtc 540
agagtggaca acagggatta taagaagtac acagtggagt gtcaggaggg cagtgcctgc 600
ccggctgccg aggagagcct acccattgaa gtcgtgggtg acgctattca caagctcaag 660
tacgaaaact acaccagcag cttcttcctc agggacatca tcaaaccgga cccacccaag 720
aacctgcaac tgaagccatt aaaaaattct cggcatgtgg aagtgagctg ggaataacct 780
gacacctgga gcacccaca ttctacttc tccttaacat ttggcgtaaa ggtccagggc 840
aagaacaaca gagaaaagaa agacagactc tccgtggaca agacctcagc caaggtcgtg 900
tgccacaagg atgccaaagt ccgcgtgcaa gccagggacc gctactatag ctcacctctg 960
agcaactggg catccgtgtc ctgcagttag                                     990

```

<210> 9

<211> 669

<212> DNA

<213> Felis catus

<220>

<221> misc\_feature

<222> (0)...(0)

<223> Coding Sequence for SEQ ID NO: 3, IL-12p35

<400> 9

```

atgtgcccgc cgctggcct cctccttgta accatcctgg tcctgttaaa ccacctggac 60
cacctcagtt tggccaggaa cctccccaca cccacaccaa gcccaggaaat gttccagtgc 120
ctcaaccact cccaaaccct gctgcgagcc atcagcaaca cgcttcagaa ggccagacaa 180
actctagaat tttacccttg cacttcggaa gagattgatc atgaagatat cacaaaagat 240
aaaaccagca cagtggaggc ctgcttacca ctggaattag ccatgaatga gagttgcctg 300

```

```

gcttcagag agatctctct gataactaat gggagttgcc tgggtgtccag aaagacctct 360
tttatgacga ccctgtgcct tagcagtatc tatgaggact tgaagatgta ccaggtggag 420
ttcaaggcca tgaatgcaaa gctgttaatg gatcctaaaa ggcagatctt tctggatcaa 480
aacatgctga cagctattga tgagctgatg caggccctga atttcaacag tgtgactgtg 540
ccacagaact cctcccttga agaaccggat ttttataaaa ctaaaatcaa gctctgcata 600
cttcttcatg ctttcagaat ccgtgcagtg accatcaata gaatgatgag ctatctgaat 660
gcttcctag                                     669

```

<210> 10

<211> 390

<212> DNA

<213> Felis catus

<220>

<221> misc\_feature

<222> (0)...(0)

<223> Coding Sequence for SEQ ID NO:4, IL-16

<400> 10

```

atgcccgacc tcaactcctc cactgattct acaaactcgg cttctgtggc cagcgacgtt 60
tctggggatt ccacggaggc cacggtgcac acggtgacgc tggagaagac gtccgcgggg 120
ctgggcttca gcctggaagg cggcaagggc tccctgctcg gggacaagcc tctcacctg 180
aacaggattt tcaaaggggc agcctcggaa cagagcgaga cgatccagcc gggagatgaa 240
atcttacact tggccggcac tgccgtgcag gggctcacgc ggtttgaagc ctggaacgtt 300
atcaagacgt tgctgacgg ccccgtcacg atcgatca gaggagaag cgtccagtcc 360
tcgggaacca cagctgctgg agactcctag                                     390

```

01-10-02 74/030520

JG10 Rec'd PCT/PTO 08 JAN 2002

#4

PATENT

Attorney's Docket No. 33339/242753

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

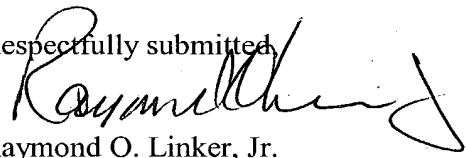
In re: Leutenegger, et al. Attn: DO/US  
International Appl. No.: PCT/DE00/02262  
International Filing Date: July 8, 2000  
For: Vaccine Against Lentiviral Infections,  
Such As The Feline Immune Deficiency  
Virus Of The Cat

U.S. Patent and Trademark Office  
Box Sequence  
P.O. Box 2327  
Arlington, VA 22202  
January 8, 2002

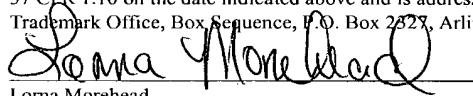
**STATEMENT IN SUPPORT OF FILING A  
SEQUENCE LISTING UNDER 37 CFR § 1.821(f)**

Sir:

I hereby state that the content of the paper and computer readable copies of the Sequence Listing, submitted concurrently herewith in accordance with 37 CFR § 1.821(c) and (e), are the same.

Respectfully submitted,  
  
Raymond O. Linker, Jr.  
Attorney/Agent for Applicant  
Registration No. 26,419

**Customer No. 00826**  
**Alston & Bird LLP**  
Bank of America Plaza  
101 South Tryon Street, Suite 4000  
Charlotte, NC 28280-4000  
Tel Raleigh Office (919) 862-2200  
Fax Raleigh Office (919) 862-2260

<p><b>"Express Mail" Mailing Label Number EL 822757496 US</b> Date of Deposit: January 8, 2002</p> <p>I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to U.S. Patent &amp; Trademark Office, Box Sequence, P.O. Box 2327, Arlington, VA 22202</p> <p> Lorna Morehead</p>	<p><b>CERTIFICATE OF MAILING</b></p> <p>I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner For Patents, Washington, DC 20231, on January 8, 2002.</p>
---	---

SEQUENCE LISTING

<110> Leutenegger, Christian  
 Schroff, Mattias  
 Willig, Burghardt  
 Lutz, Hans

<120> Vaccine Against Lentiviral Infections,  
 such as the Feline Immune Deficiency Virus of the Cat

<130> 33339/242753

<150> PCT/DE00/02262

<151> 2000-07-08

<150> CH 1258/1999

<151> 1999-07-08

<160> 10

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 5871

<212> DNA

<213> Feline lentiviruses

<220>

<221> misc\_feature

<222> (0)...(0)

<223> FIV gp140 (pMOLFIVgp140)

<400> 1

tcttccgctt	cctcgctcac	tgactcgctg	cgctcggtcg	ttcggctg	gcgagcggta	60
tcagctcact	caaaggcgg	aatacgggta	tccacagaat	caggggataa	cgaggaaag	120
aacatgtgag	caaaggcca	gcaaaaggcc	aggaaccgta	aaaaggccgc	gttgctggcg	180
tttttccata	ggctccgccc	ccctgacgag	catcacaaaa	atcgacgctc	aagtcagagg	240
tggcgaaacc	cgacaggact	ataaagatac	caggcggttc	cccctggaag	ctccctcggt	300
cgctctcctg	ttccgacct	gccgcttacc	ggatacctgt	ccgcctttct	cccttcggga	360
agcgtggcgc	tttctcatag	ctcacgctgt	aggtatctca	gttcgggtgta	ggtcgttcgc	420
tccaagctgg	gctgtgtgca	cgaaccccc	gttcagcccc	accgctgcgc	cttatccggg	480
aactatcgtc	ttgagtccaa	cccggtaaga	cacgacttat	cgccactggc	agcagccact	540
ggtaacacga	ttagcagagc	gagggtatgta	ggcggtgcta	cagagttctt	gaagtgggtg	600
cctaactacg	gctacactag	aaggacagta	tttggtatct	gcgctctgct	gaagccagtt	660
accttcggaa	aaagagttgg	tagctcttga	tccggcaaac	aaaccaccgc	tggtagcggg	720
ggtttttttg	tttgcaagca	gcagattacg	cgcagaaaaa	aaggatctca	agaagatcct	780
ttgatctttt	ctacgggggtc	tgacgctcag	tggaacgaaa	actcacgtta	agggattttg	840
gtcatgagat	tatcaaaaag	gatcttcacc	tagatccttt	taaattaaaa	atgaagtttt	900
aaatcaatct	aaagtatat	tgagtaaaact	tggtctgaca	gttaccaatg	cttaatcagt	960
gaggcaccta	tctcagcgat	ctgtctatct	cggtcatcca	tagttgcctg	actccccgtc	1020
gtgtagataa	ctacgatacg	ggaggggctta	ccatctggcc	ccagtgtctg	aatgataacc	1080
cgagaccac	gctcaccggc	tccagattta	tcagcaataa	accagccagc	cggaagggcc	1140
gagcgcagaa	gtggctcctg	aactttatcc	gcctccatcc	agtctattaa	ttgttgccgg	1200
gaagctagag	taagtagttc	gccagttaat	agtttgcgca	acgttggttg	cattgctaca	1260

```

ggcatcgctgg tgtcacgctc gtcgtttggg atggcttcat tcagctccgg ttcccaacga 1320
tcaaggcgag ttacatgatc ccccatgttg tgcaaaaaag cggtttagctc ctccggtcct 1380
ccgatcgctg tcagaagtaa gttggccgca gtgttatcac tcatggttat ggcagactg 1440
cataattctc ttactgtcat gccatccgta agatgctttt ctgtgactgg tgagtactca 1500
accaagtcac tctgagaata gtgtatgctg cgaccgagtt gctcttgccc ggcgtcaata 1560
cgggataata ccgcgccaca tagcagaact ttaaaagtgc tcatcattgg aaaacgttct 1620
tcggggcgaa aactctcaag gatcttaccg ctgttgagat ccagttcgat gtaacccact 1680
cgtgcaccca actgatcttc agcatctttt actttcacca gcgtttctgg gtgagcaaaa 1740
acaggaaaggc aaaatgccgc aaaaaaggga ataaggcgca cacggaaatg ttgaatactc 1800
atactcttcc tttttcaata ttattgaagc atttatcagg gttattgtct catgagcgga 1860
tacatatattg aatgtattta gaaaaataaa caaatagggg ttccgcgcac atttccccga 1920
aaagtgccac ctgacgtcta agaaaccatt attatcatga cattaacctt taaaaatagg 1980
cgtatcacga ggcccttttcg tctcgcgctt ttccggtgatg acggtgaaaa cctctgacac 2040
atgcagctcc cggagacggg cacagcttgt ctgtaagcgg atgccgggag cagacaagcc 2100
cgtcagggcg cgtcagcggg tgttgccggg ctgctgggct ggcttaacta tgcggcatca 2160
gagcagattg tactgagagt gcaccatag cgggtgtgaaa taccgcacag atgcgtaagg 2220
agaaaaatacc gcacagggcg ccattcgcca ttcaggctgc gcaactgttg ggaagggcgga 2280
tcggtgcggg cctcttcgct attacgccag ctggcgaaag ggggatgtgc tgcaaggcga 2340
ttaagtggg taacgccagg gttttcccag tcacgacggt gtaaaacgac ggccagtgcc 2400
aagcttgcca attctggatc cgctagctta accgtattac cgccatgcat tagttattaa 2460
tagtaatacaa ttacgggggtc attagttcat agcccatata tggagttccg cgttacataa 2520
cttacggtaa atggcccgcg tggtgacccg cccaacgacc ccgcccatt gacgtcaata 2580
atgacgtatg ttcccatagt aacgccaata gggactttcc attgacgtca atgggtggag 2640
tatttacggt aaactgcccc cttggcagta catcaagtgt atcatatgcc aagtacgccc 2700
cctattgacg tcaatgacgg taaatggccc gcctggcatt atgccagta catgacctta 2760
tgggactttc ctacttgcca gtacatctac gtattagtca tcgctattac catgggtgatg 2820
cggttttggc agtacatcaa tgggcgtgga tagcggtttg actcacgggg atttccaagt 2880
ctccacccca ttgacgtcaa tgggagtttg ttttggcacc aaaatcaacg ggactttcca 2940
aaatgtcgta acaactccgc cccattgacg caaatgggcg gtaggcgtgt acggtgggag 3000
gtctatataa gcagagctgg tttagtgaac cgtcagatgg taccatggca gaagatttg 3060
cagccaatag acaatggata gggccagaag aagctgaagg gttgttagat tttgatatag 3120
caacacaaat gaatgaagaa gggccactaa atccaggaat aaaccattt aggggtgctg 3180
gaatagcaga aatagaaaag cgagactatt gcaaaatatt acaaccaaa ttacaagatc 3240
taaagaatga aattcaagag gtaaaactgg aagaaggaaa tgcaggtaag tttagaagag 3300
caagattttt aagatattct gatgaaaata tattatccct gattcatttg ttcatagggg 3360
attgtacata tttatgcaga aaaaatgagt taggatcttt acgacatgac atagatatag 3420
acgaacatca agaagagtat tatactagta tagagaaaag tacaactgcc aatataaaat 3480
atggtagacg atgtctcata ggaacagcgg ctttgtacct gcttttcata ggaataaaat 3540
tatatacaca aacaaccaag gctcaggtag tatggagact tccaccatta gtagtccccg 3600
tgaaagaatc agagataatt ttttgggatt gttgggcacc agaggaaccc gcctgtcagg 3660
actttcttgg ggcaatgata catctaaaag ctagtacaaa tataagtata caagagggac 3720
ctaccctggg gaattgggct agagaaatat ggggaacatt attcaaaaag gctaccagac 3780
aatgtagaag aggtagagta tggagaagat ggaatgagac tataacagga ccatcaggat 3840
gtgctaataa cacatgttat aatatctcag taatagtacc tgattatcaa tgttatttag 3900
acagagtaga tacttggtta caagggaag taaatatatc attatgtcta acaggaggaa 3960
aaatgttgta taataaatat acaaaaacaat tgagctattg tacagatcca ttacaaatcc 4020
cactgatcaa ttatacgttt ggacctaatc aaacatgtaa gtggaacact tcacagattc 4080
aagactctga gataccaaaa tgtggatggg ggaatcaagc agcctattat aacagttgta 4140
gatgggaaag cactgatgta aagtttctatt gtcaaagaac acagagtctg cctggaacat 4200
ggcttagaac aatctcatca tggaggccaa agaatagatg ggaatggagg ccagattttg 4260
aaagtgaaaa agtgaaaagta tctctacagt gtaatagcac aagcaacctt acctttgcaa 4320
tgagaagttc aggagattat ggagaggtaa cgggagcatg gatagaattt ggatgtcata 4380
ggaaaaaatc aaaaacttcat tctgaagcaa ggtttagaat cagatgtaga tgggataaaag 4440
gggataatac ctactcatt gatacatgtg gaaaaactca aaatgtttta ggtgcaaadc 4500
ctgtagattg caccatgtat gcaaatagaa tgtataattg ttccttacia aatgggttta 4560
ctatgaagat agatgacctt gttatgcatt tcaatatgac gaaagctgta gaaatgtata 4620
acattgctgg aaattgggtc tgtacatctg acttgccacc aacatggggg tatatgaatt 4680

```

```

gtaattgtac aaatagtagt agtacaacta gtagttctgg taataaaatg gcatgtcctg 4740
gagataaagg tatcttaaga aattggtata acccagtagc aggattaaga caatccctag 4800
aaaagtatca agtagtaaaa caaccagatt acttagtggt gccaggggaa gtcatggaat 4860
ataaacctag aaggaaaaga gcagctattc atgttatggt agctcttgca acagtattat 4920
ctatggcccg ggcaggggac ggggctactg ctatagggat ggtaacgcaa tatcaccaag 4980
ttctggcaac tcatcaagaa gctatagaaa aggtgactga agccttaaag ataaacaact 5040
taagattagt tacattagag catcaagtac tagtaatagg attaaaagta gaagctatgg 5100
aaaaattttt atatacagct ttcgctatgc aagaattagg atgtaatcaa aatcaattct 5160
tctgtaaaagt cctcctgtg ttgtgggaaa gatataatat gactataaat caaacaatat 5220
ggaatcatgg aaatataact ttgggggaat ggtataacca aacaaaagat ttacaacaaa 5280
agttctatga aataataatg gacatagaac aaaataatgt acaaggaaaa aaaggggttac 5340
aacaattaca aaaatgggaa gattgggtag gatggatagg aaatattcca aaatatttat 5400
aagagctcat aatcagccat accacatttg tagaggtttt acttgcttta aaaaacctcc 5460
cacacctccc cctgaacctg aaacataaaa tgaatgcaat tcttggtggt aacttggtta 5520
ttgcagctta taatgggtac aaataaagca atagcatcac aaatttcaca aataaagcat 5580
ttttttcact gcattctagt tgtggtttgt ccaaaactcat caatgtatct taacgcgaat 5640
tcgtaatcat ggctatagct gtttctctgt tgaaattggt atccgctcac aattccacac 5700
aacatacgag ccggaagcat aaagtgtaaa gcctgggggt cctaataagt gagctaactc 5760
acattaattg cgttgcgctc actgcccgtt tccagtcgg gaaacctgtc gtgccagctg 5820
cattaatgaa tcggccaacg cgcggggaga ggcggtttgc gtattgggcg c 5871

```

<210> 2

<211> 4522

<212> DNA

<213> Felis catus

<220>

<221> misc\_feature

<222> (0)...(0)

<223> IL-12p40

<400> 2

```

tcttccgctt cctcgcctac tgactcgtg cgctcggctg ttcggctgcg gcgagcggta 60
tcagctcact caaaggcggg aatacgggta tccacagaat caggggataa cgcaggaaag 120
aacatgtgag caaaaggcca gcaaaaggcc aggaaccgta aaaaggccgc gttgctggcg 180
tttttccata ggctccgccc ccctgacgag catcacaaaa atcgacgctc aagtcagagg 240
tggcgaaacc cgacaggact ataaagatac caggcggtttc cccctggaag ctccctcgtg 300
cgctctcctg ttccgacctt gccgcttacc ggatacctgt ccgcctttct cccttcggga 360
agcgtggcgc tttctcatag ctacgctgt aggtatctca gttcgggtga ggtcgttcgc 420
tccaagctgg gctgtgtgca cgaaccccc gttcagcccc accgctgcg cttatccggg 480
aactatcgtc ttgagtccea ccgggtaaga cagcacttat cgccactggc agcagccact 540
ggtaacagga ttagcagagc gaggtatgta ggcggtgcta cagagttctt gaagtgggtg 600
cctaactacg gctacactag aaggacagta tttggtatct gcgctctgct gaagccagtt 660
accttcggaa aaagagttgg tagctcttga tccggcaaac aaaccaccgc tggtagcggg 720
gggttttttg tttgcaagca gcagattacg cgcagaaaaa aaggatctca agaagatcct 780
ttgatctttt ctacgggggtc tgacgctcag tggaacgaaa actcacgtta agggattttg 840
gtcatgagat tatcaaaaag gatcttcacc tagatccttt taaattaaaa atgaagtttt 900
aaatcaatct aaagtatata tgagtaaaact tggcttgaca gttaccaatg cttaatcagt 960
gaggcaccta tctcagcgat ctgtctattt cgttcatcca tagttgctg actccccgtc 1020
gtgtagataa ctacgatagc ggagggttta ccattgggcc ccagtgtgc aatgataaccg 1080
cgagacccac gctcaccggc tccagattta tcagcaataa accagccagc cggaagggcc 1140
gagcgcagaa gtggctcctgc aactttatcc gcctccatcc agtctattaa ttgttgccgg 1200
gaagctagag taagtagttc gccagttaat agtttgcgca acgttggtgc cattgctaca 1260
ggcatcgtgg tgtaacgctc gtcgtttggg atggcttcat tcagctccgg ttcccaacga 1320
tcaaggcgag ttacatgata ccccatgttg tgcaaaaaag cgggttagctc cttcggtcct 1380

```



```

ccgatcgttg tcagaagtaa gttggccgca gtgttatcac tcatggttat ggcagcactg 1440
cataattctc ttactgtcat gccatccgta agatgctttt ctgtgactgg tgagtactca 1500
accaagtcac tctgagaata gtgtatgcgg cgaccgagtt gctcttgccc ggcgtcaata 1560
cgggataata ccgcgccaca tagcagaact ttaaaagtgc tcatcattgg aaaacgttct 1620
tcggggcgaa aactctcaag gatcttaccg ctgttgagat ccagttcgat gtaacccact 1680
cgtgcaccca actgatcttc agcatctttt actttcacca gcgtttctgg gtgagcaaaa 1740
acaggaaggc aaaatgccgc aaaaaaggga ataaggcgca cacggaaatg ttgaatactc 1800
atactcttcc tttttcaata ttattgaagc atttatcagg gttattgtct catgagcgga 1860
tacatatattg aatgtatttta gaaaaataaa caaatagggg ttcgcgcac atttccccga 1920
aaagtgccac ctgacgtcta agaaaccatt attatcatga cattaaccta taaaaatagg 1980
cgtatcacga ggccctttcg tctcgcgcgt ttcgggtgatg acggtgaaaa cctctgacac 2040
atgcagctcc cggagacggg cacagcttgt ctgtaagcgg atgccgggag cagacaagcc 2100
cgtcagggcg cgtcagcggg tgttggcggg tgcgggggt ggcttaacta tgcggcatca 2160
gagcagattg tactgagagt gcaccatata cgggtgtgaaa taccgcacag atgcgtaagg 2220
agaaaatacc gcatacggcg ccattcgcca ttcaggctgc gcaactgttg ggaaggcgca 2280
tcggtgcggg cctcttcgct attacgccag ctggcgaaag ggggatgtgc tgcaaggcga 2340
ttaagtggg taacgccagg gttttcccag tcacgacgtt gtaaaacgac ggccagtgcc 2400
aagcttggtc tccccctgga tccgctagct taaccgtatt accgccatgc attagttatt 2460
aatagtaatc aattacgggg tcattagttc atagcccata tatggagttc cgcgttacat 2520
aacttacggg aaatggcccc cctggctgac cgcccaacga cccccgcca ttgacgtcaa 2580
taatgacgta tgttcccata gtaacgccaa tagggacttt ccattgacgt caatgggtgg 2640
agtatttacg gtaaaactgcc cacttggcag tatatcaagt gtatcatatg ccaagtacgc 2700
cccctattga cgtcaatgac ggtaaatggc ccgcctggca ttatgccag tacatgacct 2760
tatgggactt tctactttgg cagtacatct acgtattagt catcgctatt accatgggtga 2820
tgcggttttg gcagtacatc aatgggcgtg gatagcgggt tgactcacgg ggatttccaa 2880
gtctccaccc cattgacgtc aatgggagtt tgttttggca ccaaaatcaa cgggactttc 2940
caaaatgtcg taacaactcc gccccattga cgcaaattgg cggtaggcgt gtacgggtgg 3000
aggtctatat aagcagagct ggttttagtga accgtcagat ggtaccatgc atcctcagca 3060
gttggtcata gcctgggttt ccctgggttt gctggcacct cccctcatgg ccataaggga 3120
actggagaaa aacgtttatg ttgtagagtt ggactggcac cctgatgccc ccgagaaat 3180
ggtggtcctt acctgcaata ctctgaaga agatgacatc acctggacct ctgaccagag 3240
cagtgaagtc ctaggctctg gtaaaactct gaccatccaa gtcaaagaat ttgcagatgc 3300
tgccagat acctgtcata aaggaggcga ggttctgagc cattcgttcc tctgataca 3360
caaaaaggaa gatggaattt ggtccactga tatcttaagg gaacagaaag aatccaaaaa 3420
taagatcttt ctaaaatgtg aggcaaagaa ttattctgga cgtttcacct gctggtggct 3480
gacggcaatc agtaccgatt tgaaattcac tgtcaaaagc agcagaggct cctctgacct 3540
ccaaggggtg acttgtggag cagcgacact ctacgcagag aaggtcagag tggacaacag 3600
ggattataag aagtacacag tggagtgtca ggaggcaggt gcctgcccgg ctgccgagga 3660
gagcctaccc attgaagtcg tgggtggacgc tattcacaag ctcaagtacg aaaactacac 3720
cagcagcttc ttcatcaggg acatcatcaa accggaccca cccaagaacc tgcaactgaa 3780
gccattaaaa aattctcggc atgtggaagt gagctgggaa taccctgaca cctggagcac 3840
cccacattcc tacttctcct taacatttgg cgtacaggtc cagggaaga acaacagaga 3900
aaagaaagac agactctccg tggacaagac ctacagccaag gtcgtgtgcc acaaggatgc 3960
caagatccgc gtgcaagcca gggaccgcta ctatagctca tcctggagca actgggcatc 4020
cgtgtcctgc agttaggagc tcataatcag ccataccaca tttgtagagg ttttacttgc 4080
tttaaaaaac ctcccacacc tccccctgaa cctgaaacat aaaatgaatg caattcttgt 4140
tgtaacttgg tttatttgag cttataatgg ttacaaataa agcaatagca tcacaaattt 4200
cacaaataaa gcattttttt cactgcattc tagttgtggt ttgtccaaac tcatcaatgt 4260
atcttaacgc gaattcaggg ggagacccaa ttcgtaatca tgggtcatagc tgtttcctgt 4320
gtgaaattgt tatccgctca caattccaca caacatacga gccggaagca taaagtgtaa 4380
agcctggggg gcctaattgag tgagctaact cacattaatt gcgttgcgct cactgcccgc 4440
tttccagtcg ggaaacctgt cgtgccagct gcattaatga atcgccaac gcgcggggag 4500
aggcggtttg cgtattgggc gc 4522

```

```

<210> 3
<211> 4201
<212> DNA

```

<213> Felis catus

<220>

<221> misc\_feature

<222> (0)...(0)

<223> IL-12p35 (pMOLfIL-12p35 (e-,\_e31-) clone 61)

<400> 3

```
tcttccgctt cctcgctcac tgactcgctg cgctcggtcg ttcggctgcg gcgagcggta 60
tcagctcact caaaggcggg aatacgggta tccacagaat caggggataa cgcaggaaag 120
aacatgtgag caaaaggcca gcaaaaggcc aggaaccgta aaaaggccgc gttgctggcg 180
tttttccata ggctccgccc ccctgacgag catcacaaaa atcgacgctc aagtcagagg 240
tggcgaaaacc cgacaggact ataaagatac caggcggttc cccctggaag ctccctcgctg 300
cgctctcctg ttccgacctt gccgcttacc ggatacctgt ccgcctttct cccttcggga 360
agcgtggcgc ttctcatag ctacgctgt aggtatctca gttcgggtga ggtcgcttcgc 420
tccaagctgg gctgtgtgca cgaaccccc gttcagcccc accgctgcgc cttatccggt 480
aactatcgtc ttgagtccaa cccggtaaga cagcacttat cgccactggc agcagccact 540
ggtaacagga ttagcagagc gaggtatgta ggcgggtgcta cagagttctt gaagtgggtg 600
cctaactacg gctacactag aaggacagta tttgggtatct gcgctctgct gaagccagtt 660
accttcggaa aaagagttgg tagctcttga tccggcaaac aaaccaccgc tggtagcggg 720
ggtttttttg tttgcaagca gcagattacg cgcagaaaaa aaggatctca agaagatcct 780
ttgatctttt ctacggggtc tgacgctcag tggaacgaaa actcacgta agggattttg 840
gtcatgagat tatcaaaaag gatcttcacc tagatccttt taaattaaaa atgaagtttt 900
aaatcaatct aaagtatata tgagtaaaact tggcttgaca gttaccaatg cttaatcagt 960
gaggcaccta tctcagcgat ctgtctatct cgttcatcca tagttgcctg actccccgctc 1020
gtgtagataa ctacgatacg ggagggttta ccatctggcc ccagtgcctg aatgataccg 1080
cgagaccacg gctcaccggc tccagattta tcagcaataa accagccagc cggaagggcc 1140
gagcgcagaa gtggctcctg aactttatcc gcctccatcc agtctattaa ttgttgccgg 1200
gaagctagag taagtagttc gccagttaat agtttgcgca acggtgttgc cattgctaca 1260
ggcatcgtgg tgtcacgctc gtcgtttggt atgggttcat tcagctccgg tccccagcga 1320
tcaaggcggg ttacatgata ccccatggtg tgcaaaaaag cggttagctc cttcggctct 1380
ccgatcgttg tcagaagtaa gttggccgca gtgttatcac tcatggttat ggcagcactg 1440
cataattctc ttactgtcat gccatccgta agatgctttt ctgtgactgg tgagtactca 1500
accaagtcac tctgagaata gtgtatgcgg cgaccgagtt gctcttgccc ggcgtcaata 1560
cgggataata ccgcgccaca tagcagaact ttaaaagtgc tcatcattgg aaaacgttct 1620
tcggggcgaa aactctcaag gatcttaccg ctgttgagat ccagttcgat gtaaccact 1680
cgtgcaccca actgatcttc agcatctttt actttacca gcgtttctgg gtgagcaaaa 1740
acaggaaagg aaaaagcgcg aaaaaaggga ataaggcgca cacggaaatg ttgaatactc 1800
atactcttcc tttttcaata ttattgaagc atttatcagg gttattgtct catgagcgga 1860
tacatatattg aatgtattta gaaaaataaa caaatagggg ttccgcgcac atttccccga 1920
aaagtgccac ctgacgtcta agaaaccatt attatcatga cattaaccta taaaaatagg 1980
cgtatcacga ggccctttcg tctcgcgctg ttcgggtgat acggtgaaaa cctctgacac 2040
atgcagctcc cggagacggg cacagcttgt ctgtaagcgg atgccgggag cagacaagcc 2100
cgtcagggcg cgtcagcggg tgttggcggg tgcgggggct ggcttaacta tgcggcatca 2160
gagcagattg tactgagagt gcaccatatg cgggtgtgaaa taccgcacag atgcgtaagg 2220
agaaaaatac gcacagggcg ccattcgcca ttcaggctgc gcaactgttg ggaaggcgca 2280
tcgggtgcggg cctcttcgct attacgccag ctggcgaaag ggggatgtgc tgcaaggcga 2340
ttaagtggg taacgccagg gttttcccag tcacgacgtt gtaaaacgac ggccagtgcc 2400
aagcttggtc tccccctgga tccgctagct taaccgtatt accgccatgc attagttatt 2460
aatagtaatc aattacgggg tcattagttc atagcccata tatggagttc cgcgttacat 2520
aacttacggg aaatggcccc cctggctgac cgcccaacga cccccgcca ttgacgtcaa 2580
taatgacgta tgttcccata gtaacgccaa tagggacttt ccattgacgt caatgggtgg 2640
agtattttacg gtaaacctgc cacttggcag tacatcaagt gtatcatatg ccaagtacgc 2700
cccctattga cgtaaatgac ggtaaatgac ccgcctggca ttatgccag tacatgacct 2760
tatgggactt tcctacttgg cagtacatct acgtattagt catcgctatt accatgggtga 2820
tgcggttttg gcagtacatc aatgggcgtg gatagcgggt tgactcacgg ggatttccaa 2880
gtctccaccc cattgacgct aatgggagtt tgttttggca ccaaaatcaa cgggactttc 2940
```

```

caaaatgtcg taacaactcc gccccattga cgcaaattggg cggtaggcgt gtacgggtggg 3000
agggtctatat aagcagagct ggttttagtga accgtcagat ggtaccatgt gcccgcgcgcg 3060
tggcctcctc cttgtaacca tcctggteet gttaaaccac ctggaccacc tcagtttggc 3120
caggaacctc cccacaccca caccaagccc aggaatgttc cagtgcctca accactccca 3180
aaccctgctg cgagccatca gcaacacgct tcagaaggcc agacaaactc tagaatttta 3240
ccccgcaact tccgaagaga ttgatcatga agatatcaca aaagataaaa ccagcacagt 3300
ggaggcctgc ttaccactgg aattagccat gaatgagagt tgcctggctt ccagagagat 3360
ctctctgata actaatggga gttgcctggt gtccagaaag acctctttta tgacgaccct 3420
gtgccttagc agtatctatg aggacttgaa gatgtaccag gtggagtcca aggccatgaa 3480
tgcaaagctg ttaatggatc ctaaaaggca gatctttctg gatcaaaaca tgctgacagc 3540
tattgatgag ctgatgcagg ccctgaattt caacagtgtg actgtgccac agaactcctc 3600
ccttgaagaa ccggattttt ataaaactaa aatcaagctc tgcatacttc ttcattgctt 3660
cagaatccgt gcagtgaacca tcaatagaat gatgagctat ctgaatgctt cctaggagct 3720
cataatcagc cataccacat ttgtagaggt tttacttgct ttaaaaaacc tcccacacct 3780
ccccctgaac ctgaaacata aaatgaatgc aattgttggt gttaacttgt ttattgcagc 3840
ttataatggt taaaaataaa gcaatagcat cacaatttcc acaataaaag catttttttc 3900
actgcattct agttgtggtt tgtccaaact catcaatgta tcttaacgcg aattcagggg 3960
gagacccaat tcgtaatcat ggtcatagct gtttctctgt tgaaatttgt atccgctcac 4020
aattccacac aacatacgag ccggaagcat aaagtgtaaa gcctgggggtg cctaattgagt 4080
gagctaactc acattaattg cgttgcgctc actgcccgtc ttccagtcgg gaaacctgtc 4140
gtgccagctg cattaatgaa tcggccaacg cgcggggaga ggcggtttgc gtattgggag 4200
c 4201

```

```

<210> 4
<211> 3903
<212> DNA
<213> Felis catus

```

```

<220>
<221> misc_feature
<222> (0)...(0)
<223> IL-16

```

```

<400> 4
tcttccgctt cctcgcctcac tgactcgcgt cgctcggctc ttcggctgcg gcgagcggta 60
tcagctcact caaaggcggg aatacgggta tccacagaat caggggataa cgcaggaaag 120
aacatgtgag caaaaggcca gcaaaaggcc aggaaccgta aaaaggccgc gttgctggcg 180
ttttccata ggtccgccc cctgacgag catcacaaaa atcgacgctc aagtcagagg 240
tggcgaaaacc cgacaggact ataaagatac caggcgtttc cccctggaag ctccctcgtg 300
cgctctcctg ttccgacct gccgcttacc ggatacctgt ccgcctttct cccttcggga 360
agcgtggcgc tttctcatag ctacgcgtgt aggtatctca gttegggtga ggtcgttcgc 420
tccaagctgg gctgtgtgca cgaaccccc gtccagccc accgctgcgc cttatccggt 480
aactatcgtc ttgagtccaa cccggtaaga cagcacttat cgccactggc agcagccact 540
ggtaacagga ttagcagagc gaggtatgta ggcggtgcta cagagttctt gaagtgggtg 600
cctaactacg gctacactag aaggacagta tttggtatct gcgctctgct gaagccagtt 660
accttcggaa aaagagttgg tagctcttga tccggcaaac aaaccaccgc tggtagcggg 720
ggtttttttg tttgcaagca gcagattacg cgcagaaaaa aaggatctca agaagatcct 780
ttgatctttt ctacgggggtc tgacgctcag tggaaacgaaa actcacgtta agggattttg 840
gtcatgagat tatcaaaaag gatcttcacc tagatccttt taaattaaaa atgaagtttt 900
aaatcaatct aaagtatata tgagtaaact tgggtctgaca gttaccaatg cttaatcagt 960
gaggcaccta tctcagcgat ctgtctatct cgttcatcca tagttgcctg actccccgtc 1020
gtgtagataa ctacgatacg ggagggtcta ccacttgccc ccagtgtgc aatgataacc 1080
cgagacccac gctcacggc tccagattta tcagataata accagccagc cggaagggcc 1140
gagcgcagaa gtgggtcctgc aactttatcc gcctccatcc agtctattaa ttgttgcggg 1200
gaagctagag taagtagttc gccagttaat agtttgcgca acgttggtgc cattgctaca 1260
ggcatcgtag tgcacgctc gtcgtttggt atggcttcat tcagctccgg ttcccaacga 1320
tcaaggcgag ttacatgac ccccatggtg tgcaaaaaag cggttagctc cttcgggtcct 1380

```

```

ccgacgcttg tcagaagtaa gttggccgca gtgttatcac tcatggttat ggcagcactg 1440
cataattctc ttactgtcat gccatccgta agatgctttt ctgtgactgg tgagtactca 1500
accaagtcac tctgagaata gtgtatgcgg cgaccgagtt gctcttgccc ggcgtcaata 1560
cgggataata ccgcgccaca tagcagaact ttaaaagtgc tcatcattgg aaaacgttct 1620
tcggggcgaa aactctcaag gatcttaccg ctgttgagat ccagttcgat gtaacccact 1680
cgtgcaccca actgatcttc agcatctttt actttcacca gcgtttctgg gtgagcaaaa 1740
acaggaaggc aaaatgccgc aaaaaaggga ataagggcga cacggaaatg ttgaatactc 1800
atactcttcc tttttcaata ttattgaagc atttatcagg gttattgtct catgagcgga 1860
tacatatttg aatgtattta gaaaaataaa caaatagggg ttccgcgcac atttccccga 1920
aaagtgccac ctgacgtcta agaaaccatt attatcatga cattaacctt taaaaatagg 1980
cgtatcacga ggccttttcg tctcgcgcgt ttcggtgatg acggtgaaaa cctctgacac 2040
atgcagctcc cggagacggg cacagcttgt ctgtaagcgg atgccgggag cagacaagcc 2100
cgtcagggcg cgtcagcggg tgttggcggg tgcgggggct ggcttaacta tgcggcatca 2160
gagcagattg tactgagagt gcaccatatg cgggtgtgaa taccgcacag atgcgtaagg 2220
agaaaatacc gcatcaggcg ccattcgcca ttcaggctgc gcaactgttg ggaagggcga 2280
tcggtgccgg cctcttcgct attacgccag ctggcgaaag ggggatgtgc tgcaaggcga 2340
ttaagttggg taacgccagg gttttcccag tcacgacgtt gtaaaacgac ggccagtgcc 2400
aagcttgcca attctggatc cgctagctta accgtattac cgccatgcat tagttattaa 2460
tagtaatcaa ttacggggtc attagttcat agcccatata tggagttccg cgttacataa 2520
cttacggtaa atggcccgcg tggtgaccg cccaacgacc ccgcccatt gacgtcaata 2580
atgacgtatg ttcccatagt aacgcccaata gggactttcc attgacgtca atgggtggag 2640
tatttacggg aaactgcccc cttggcagta atcagtggt atcatatgcc aagtacgcc 2700
cctattgacg tcaatgacgg taaatggccc gcctggcatt atgccagta catgacctta 2760
tgggactttc ctacttggca gtacatctac gtattagtca tcgctattac catggtgatg 2820
cgggttttggc agtacatcaa tgggcgtgga tagcggtttg actcacgggg atttccaagt 2880
ctccaccca ttgacgtcaa tgggagtttg ttttggcacc aaaatcaacg ggactttcca 2940
aaatgtcgta acaactccgc ccattgacg caaatgggcg gtaggcgtgt acggtgggag 3000
gtctatataa gcagagctgg tttagtgaac cgtcagatgg taccatgccc gacctcaact 3060
cctccactga ttctacaaac tcggcttctg tggccagcga cgtttctggg gattccacgg 3120
agggcacggg gcacacggtg acgctggaga agacgtccgc ggggctggg ttcagcctgg 3180
aaggcggcaa gggctccctg ctccgggaca agcctctcac cgtgaacagg attttcaaag 3240
gggcagcctc ggaacagagc gagacgatcc agccgggaga tgaaatctta cacttggccg 3300
gcactgccgt gcaggggctc acgcggtttg aagcctggaa cgttatcaag acgttgccctg 3360
acggccccgt cacgatcgtc atcaggagga gaagcgtcca gtcctcgga accacagctg 3420
ctggagactc ctaggagctc ataatacagc ataccacatt tgtagagggt ttacttgctt 3480
taaaaaacct cccacacctc cccctgaacc tgaaacataa aatgaatgca attcttggtg 3540
ttaacttggt tattgcagct tataatgggt acaaataaag caatagcatc acaaatttca 3600
caaataaagc atttttttca ctgcattcta gttgtggttt gtccaaactc atcaatgtat 3660
cttaacgcga attcgtaatc atggtcatag ctgtttcctg tgtgaaattg ttatccgctc 3720
acaattccac acaacatacg agccggaagc ataaagtgtg aagcctgggg tgcctaata 3780
gtgagctaac tcacattaat tgcgttgccg tcaactgccg ctttccagtc gggaaacctg 3840
tcgtgccagc tgcattaatg aatcggccaa cgcgcgggga gaggcggttt gcgtattggg 3900
cgc 3903

```

<210> 5

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide

<221> misc\_feature

<222> (0)...(0)

<223> CpG

<400> 5

33

```
<210> 6
<211> 35
<212> DNA
<213> Artificial Sequence
```

<220>  
<223> Oligonucleotide

```
<221> misc_feature
<222> (0) ... (0)
<223> CpG
```

```
<400> 6
gaagaacgtt ttccaatgat ttttcattgg aaaac
```

35

```
<210> 7
<211> 2358
<212> DNA
<213> Feline lentiviruses
```

```
<220>
<221> misc_feature
<222> (0)...(0)
<223> Coding Sequence for SEQ ID NO:1, FIV env Gen
```

<400> 7						
atggcagaag	gatttgcagc	caatagacaa	tggatagggc	cagaagaagc	tgaaggggttg	60
ttagattttg	atatagcaac	acaaatgaat	gaagaagggc	cactaaatcc	aggaataaac	120
ccatttaggg	tgccctggaat	agcagaaata	gaaaagcgag	actattgcaa	aatattacaa	180
cccaaattac	aagatctaaa	gaatgaaatt	caagaggttaa	aactggaaga	aggaaatgca	240
ggtaagttta	gaagagcaag	atttttaaga	tattctgatg	aaaatatatt	atccccgatt	300
catttgttca	tagggttattg	tacatattta	tgcagaaaaa	atgagttagg	atctttacga	360
catgacatag	atatagacga	acatcaagaa	gagtattata	ctagtataga	gaaaggtaca	420
actgccaaata	taaaatatgg	tagacgatgt	ctcataggaa	cagcggcctt	gtacctgctt	480
ttcataggaa	taataatata	tacacaaaca	accaaggctc	aggtagtatg	gagacttcca	540
ccattagtag	tccccgtgaa	agaatcagag	ataatTTTTT	gggattgttg	ggcaccagag	600
gaacccgcct	gtcaggactt	tcttggggca	atgatacatc	taaaagctag	tacaaatata	660
agtatacaag	agggacctac	cctggggaaat	tgggctagag	aaatatgggg	aacattattc	720
aaaaaggcta	ccagacaatg	tagaaggagt	agagttatgga	gaagatggaa	tgagactata	780
acaggaccat	caggatgtgc	taataacaca	tgttataata	tctcagtaat	agtaacctgat	840
tatcaatgtt	attttagacag	agtagatact	tggttacaag	ggaaaagtaaa	tatatcatta	900
tgtctaacag	gaggaaaaat	gttgtataat	aaatatacaa	aacaattgag	ctattgtaca	960
gatccattac	aaatcccact	gatcaattat	acgtttggac	ctaatacaac	atgtaagtgg	1020
aacacttcac	agattcaaga	ctctgagata	ccaaaatgtg	gatggtggaa	tcaagcagcc	1080
tattataaca	gttgtagatg	ggaaaagcact	gatgtaaagt	ttcattgtca	aagaacacag	1140
agtcctgctg	gaacattggct	tagaacaatc	tcatcatgga	ggccaaagaa	tagatgggaa	1200
tggaggccag	attttgaaag	tgaaaaagtg	aaagtatctc	tacagtgtaa	tagcacaaagc	1260
aacctaacct	ttgcaatgag	aagttcagga	gattatggag	aggtaacggg	agcatggata	1320
gaatttggat	gtcataggaa	aaaatcaaaa	cttcattctg	aagcaagggt	tagaatcaga	1380
tgtagatggg	ataaagggga	taataacctc	ctcattgata	catgtggaaa	aactcaaaat	1440
gttttaggtg	caaatcctgt	agattgcacc	atgtatgcaa	atagaatgta	taattgttcc	1500
ttacaaaatg	ggtttactat	gaagatagat	gaccttggtt	tgcatttcaa	tatgacgaaa	1560
gctgtagaaa	tgtataacat	tgtctggaat	tggctctgta	catctgactt	gccaccaaca	1620
tgggggtata	tgaattgtaa	ttgtacaaat	agtagtagta	caactagtag	ttctggtaat	1680
aaaatggcat	gtcctggaga	taaaggatatc	ttaagaaatt	gggtataaccc	agtagcagga	1740

```

ttaagacaat ccctagaaaa gtatcaagta gtaaaacaac cagattactt agtgggtgcca 1800
ggggaagtca tggaatataa acctagaagg aaaagagcag ctattcatgt tatgttagct 1860
cttgcaacag tattatctat ggccggggca gggacggggg ctactgctat agggatggta 1920
acgcaatatc accaagttct ggcaactcat caagaagcta tagaaaagggt gactgaagcc 1980
ttaagataa acaacttaag attagttaca ttagagcatc aagtactagt aataggatta 2040
aaagtagaag ctatggaaaa attttttatat acagctttcg ctatgcaaga attaggatgt 2100
aatcaaaatc aattcttctg taaagtcctt cctgtgttgt gggaaagata taatatgact 2160
ataaatcaaa caatatggaa tcatggaaat ataactttgg gggaaatggta taaccaaaca 2220
aaagattttac aacaaaagtt ctatgaaata ataatggaca tagaacaaaa taatgtacaa 2280
ggaaaaaaag gggttacaaca attacaaaaa tggaagatt gggtaggatg gataggaaat 2340
attccaaaat atttataa 2358

```

<210> 8

<211> 990

<212> DNA

<213> Felis catus

<220>

<221> misc\_feature

<222> (0)...(0)

<223> Coding Sequence for SEQ ID NO:2, IL-12p40

<400> 8

```

atgcatcctc agcagttggg catcgccctg ttttccctgg ttttgctggc acctcccctc 60
atggccatat ggggaactgga gaaaaacggt tatgtttagt agttggactg gcaccctgat 120
gcccccgag aaatggtggg ccttacctgc aatactcctg aagaagatga catcacctgg 180
acctctgacc agagcagtgga agtcctaggg tctggtaaaa ctctgaccat ccaagtcaaa 240
gaatttgtag atgctggcca gtatacctgt cataaaggag gcgaggttct gagccattcg 300
ttctcctga tacacaaaaa ggaagatgga atttgggtcca ctgatattct aagggaacag 360
aaagaatcca aaaataagat ctttctaaaa tgtgaggcaa agaattattc tggacgtttc 420
acctgctggg ggctgacggc aatcagtagc gatttgaaat tcaactgtcaa aagcagcaga 480
ggctcctctg acccccaagg ggtgacttgt ggagcagcga cactctcagc agagaaggtc 540
agagtggaca acagggatta taagaagtag acagtggagt gtcaggaggg cagtgcctgc 600
ccggtgcccg aggagagcct acccattgaa gtcgtgggtg acgctattca caagctcaag 660
tacgaaaact acaccagcag cttcttcctc agggacatca tcaaaccgga cccacccaag 720
aacctgcaac tgaagccatt aaaaaattct cggcatgtgg aagtgcctgc ggaataacct 780
gacacctgga gcaacccaca ttctactctc tccttaacat ttggcgtaca ggtccagggc 840
aagaacaaca gagaaaagaa agacagactc tccgtggaca agacctcagc caaggtcgtg 900
tgccacaagg atgccaagat ccgctgcaaa gccagggacc gctactatag ctcatcctgg 960
agcaactggg catccgtgtc ctgcagttag 990

```

<210> 9

<211> 669

<212> DNA

<213> Felis catus

<220>

<221> misc\_feature

<222> (0)...(0)

<223> Coding Sequence for SEQ ID NO: 3, IL-12p35

<400> 9

```

atgtgccgcg cgcgtggcct cctccttgta accatcctgg tcctgttaaa ccacctggac 60
cacctcagtt tggccaggaa cctccccaca cccacaccaa gccagggaat gttccagtag 120
ctcaaccact cccaaacctt gctgcgagcc atcagcaaca cgcttcagaa ggccagacaa 180
actctagaat ttaccacctg cacttccgaa gagattgatc atgaagatat cacaaaagat 240
aaaaccagca cagtggaggc ctgcttacca ctggaattag ccatgaatga gagttgcctg 300

```

```

gcttcagag agatctctct gataactaat gggagttgcc tgggtgtccag aaagacctct 360
tttatgacga ccctgtgcct tagcagtatc tatgaggact tgaagatgta ccagggtggag 420
ttcaaggcca tgaatgcaaa gctgttaatg gatcctaataa ggcagatctt tctggatcaa 480
aacatgctga cagctattga tgagctgatg caggccctga atttcaacag tgtgactgtg 540
ccacagaact cctcccttga agaaccggat ttttataaaa ctaaaatcaa gctctgcata 600
cttcttcatg ctttcagaat ccgtgcagtg accatcaata gaatgatgag ctatctgaat 660
gcttcctag 669

```

<210> 10

<211> 390

<212> DNA

<213> Felis catus

<220>

<221> misc\_feature

<222> (0)...(0)

<223> Coding Sequence for SEQ ID NO:4, IL-16

<400> 10

```

atgcccagacc tcaactcctc cactgattct acaaactcgg cttctgtggc cagcgacgtt 60
tctgggggatt ccacggaggc cacggtgcac acggtgacgc tggagaagac gtccgcgggg 120
ctgggcttca gcctggaagg cggcaagggc tccctgctcg gggacaagcc tctcaccgtg 180
aacaggattt tcaaaggggc agcctcggaa cagagcgaga cgatccagcc gggagatgaa 240
atcttacact tggccggcac tgccgtgcag gggctcacgc ggtttgaagc ctggaacgtt 300
atcaagacgt tgcttgacgg ccccgtcacg atcgtcatca ggaggagaag cgtccagtcc 360
tcgggaacca cagctgctgg agactcctag 390

```

1/PRTS

9.0030500 1.140002

10/030500

- 1 -

531 Rec'd PCT/

08 JAN 2002

## **Vaccination against Infections with Lentiviruses, such as Feline Immune Deficiency Virus in the Cat**

### **Description**

#### **Scientific Area**

The present invention is related to a DNA-based vaccine with which cats can be protected against the feline immune deficiency virus.

#### **Scientific Status**

5 In 1987 a virus was first isolated from domestic cats which leads to immune deficiency in infected animals (Pedersen et al., 1987). This is the feline immune deficiency virus (FIV), which, as a lentivirus, belongs to the group of the retroviruses. FIV is closely related to human immune deficiency virus (HIV), simian immune deficiency virus in monkeys (SIV), lentiviruses in horses (equine infectious anaemia virus, EIAV) and in small ruminants (Maedi-Visna virus in the sheep, MVV, and caprine arthritis encephalitis virus in the goat, CAEV), as well as bovine immune deficiency virus in the cow (BIV). Just as with HIV in man, FIV leads to a decrease in  
10 blood CD4 lymphocytes during the disease and to parallel increasing weakness in the immune system (Torten et al., 1991). When the number of blood CD4 lymphocytes has decreased below a certain level, the immune system fails totally, as a result of which the cats either die or have to be put to sleep. FIV-Infection occurs throughout the world, not only in domestic cats, but also in wild *Felidae*, such as lions in East Africa. However, the frequency of FIV infections in the domestic cat varies from country to country. In Switzerland, Germany and Austria, about 3-4% of  
20 sick cats which are taken to the vet are infected with this virus. In France and England and in some areas of the USA, the rate in sick cats is between 10 and 15%; in Japan, for example, it can be as high as 40%. FIV infection is thus an important disease which is of significance in veterinary medicine. However, aside from the veterinary aspect, FIV infection is also interesting for human medicine, as this infection is  
25 very similar to human infection with HIV and is therefore very suitable as a model for the study of HIV infection and its possible prevention and therapy (Gardner, 1991;



- 2 -

Jarrett et al., 1990). In their fight against FIV infection, vets and animal owners have until now been dependent exclusively on the detection of the infection by means of immunological tests and the separation of infected from non-infected animals. At the moment, there is no vaccination which facilitates the protection of cats against FIV infection without simultaneously inducing antibodies which lead to false positive re-  
5 actions in the test used to detect FIV infection.

Natural protection against infectious diseases is based on the recognition by cells of the adaptive immune system of structures in pathogens which they have successfully combated. Two main activities may be distinguished here. On the one hand,  
10 there is the activity of the humoral immune system, which is based on the synthesis of antibodies by B-lymphocytes. On the other hand, there is the cellular immune system, which is based primarily on the activity of T-lymphocytes. These T-lymphocytes are capable of recognising body cells infected with viruses as "foreign". Depending on its specific function, the T-cell may then either amplify and modify the  
15 signal of recognition of foreign material (T helper cells), or directly initiate the lysis of the cell which has been recognised as foreign or infected (cytotoxic T-cells). Correct cooperation between the humoral and cellular immune systems is of decisive importance for the function of the immune response. In the last ten years it has become clear that the cellular arm of the immune response is induced by the activation  
20 of so-called type 1 helper cells and the humoral arm by activation of the so-called type 2 helper cells (Mosmann et al., 1986). In keeping with these names, the cellular arm is also known as the TH1 pathway and the humoral arm as the TH2 pathway of the immune system.

To solve these problems we had recourse to immunisation with DNA (Ulmer JB et  
25 al. 1993). This method has now been intensively researched and is based on vaccination with endogenously expressed antigens, which are processed intracellularly and presented to the immune system. In comparison with attenuated or recombinant vaccines, immunisation with DNA possesses not only technical and economic advantages, but also a series of biological advantages. In particular, these include the  
30 possibility of influencing the formation of a type 1 or type 2 response, either by co-expression of suitable cytokines or by insertion of substances which mediate signal transmission.

- 3 -

A series of procedures is known for the introduction of DNA expression constructs. The ballistic transfection of target cells is described in documents WO91/00539 and EP 0 500 799. Equipment for this is disclosed in WO95/19799.

5 Vaccination by direct injection of naked DNA is disclosed in US 5,580,859, US 5,589,466 and US 5,593,972.

10 A disadvantage of the vectors used at the moment for DNA immunisation is that either vectors of viral origin are used, which can result in safety problems (Gunzburg WH und Salmons B,1995), or plasmids are used. These must admittedly be regarded as absolutely safe from the epidemiological point of view and are greatly superior to viruses from the immunological point of view. They nevertheless contain sequences which make no contribution to the activity of the immunising expression cassette. These sequences include all those needed for replication in bacteria, such as the antibiotic resistance gene, replication origins etc. The problem is extensively discussed in WO98/21322.

15 Furthermore, the development of the immune response after DNA immunisation is highly dependent on the quantity and type of inoculated DNA. Depending on the method of introduction, the immunisation may require between <1µg DNA and >100µg DNA in the mouse. With larger quantities of DNA, the quality of the immune response can be greatly influenced by the presence of ISS (ISS = immunostimulatory nucleic acid sequences), such as CpG sequences (CpG = unmethylated cytosine-guanosine), in the ampicillin resistance gene. The ISS motives were indeed discovered by chance in an experiment to control this effect (Krieg et al. (1995)). If, for instance, the "gene gun" is used to introduce very small quantities of DNA into the patient's body for immunisation, a TH2 profile is typically found in the induced immune response. If, on the other hand, naked DNA is injected into muscle, much larger quantities of DNA are used and a TH1 profile is usually found.

30 It has been known for several years that certain short nucleic acid sequences included in the immuno-stimulatory ("ISS") nucleic acid sequences can exhibit considerable physiological activity in that they intensely stimulate the effector cells of the immune system through unknown mechanisms. These ISS are only a few bases long and do not act through proteins coded on them. Most known immuno-



- 5 -

bly contribute to immunity in this way (Idziorek T, et al., 1998; Amiel et al., 1999; Zhou et al., 1997)

In spite of numerous attempts, there is at the moment no vaccine which can protect cats against this infection under field conditions and which does not interfere with the detection of the infection. It has been attempted to vaccinate cats against FIV by using FIV-infected cells which had been propagated in culture and inactivated with formalin before injection (Yamamoto et al., 1993; Yamamoto et al., 1991, see also Yamamoto: US 5,275,813, 4.1.94 and US 5,510,106, 23.4.96). Tompkins et al., US 5,413,927, describe a similar invention. Cats vaccinated in this way nevertheless developed antibodies to the different FIV virus proteins. These antibodies react with the diagnostic procedure which is now used (Tonelli, 1991), so that the test cannot be employed with such a cat to decide whether it is suffering from an infection or has been vaccinated. Several research groups have been trying for years to develop a vaccine which does not give a false-positive result with vaccinated animals and could thus be confused with an established FIV infection. The approach taken has been to examine vaccines based on the FIV envelope glycoprotein produced by genetic engineering, with suitable adjuvants. One of the inventors in the present application undertook the first experiments in this direction. No protection against a test infection was found, although the result suggested that the vaccinated animals were partially immune (Hofmann-Lehmann et al., 1995; Lutz et al., 1995). A later experiment led to clearly measurable partial immunity in one of the vaccinated groups (Leutenegger et al., 1998; Lutz et al., 1996). A further experiment was carried out in which cats were vaccinated with recombinant FIV envelope glycoprotein, which had previously been inactivated with formalin, together with lymphocytes. Different adjuvants for immunisation were investigated, but the experiments were not successful (Boretti and F., 1999). The work of other research groups on the use of recombinant envelope glycoprotein as vaccine antigen has been comprehensively documented (Huisman et al., 1998; Osterhaus et al., 1996; Richardson et al., 1997). These workers were also unsuccessful in achieving protection by using these envelope glycoproteins or the DNA which codes for it (Osterhaus et al., 1996; Richardson et al., 1997; Richardson et al., 1998).

Recombinant vaccines against FIV are also known from the patent of Wasmoen et al., US 5,849,303.

- 6 -

The use of IL-12 in man as adjuvant is known from US 5,571,515.

Instructions for the use and production of immuno-stimulatory, CpG-containing ISS is comprehensively explained in application WO 98/18810 and in the literature cited there.

- 5 Covalently capped dumb-bell shaped DNA expression constructs are described in Wittig et al. (WO 98/21322). Information disclosed in all documents mentioned should be regarded as part of the description presented here.

In spite of the many studies in this area, there is as yet no proven effective protective vaccine for cats against FIV.

- 10 The aim and intention of the present invention is therefore to prepare a vaccine for *Felidae* which is capable of inducing protection against illness after FIV infection. The vaccine should allow a distinction between vaccinated animals and diseased or infected animals on the basis of their antibody status.

#### **Description of the Invention**

- 15 According to the invention, this aim is achieved by immunising animals, particularly mammals such as cats, with a DNA sequence which codes for the envelope glycoprotein and also contains a part of the gene for the transmembrane protein. In a favoured embodiment of the invention, suitable adjuvants are added to the vaccine mixture to evoke a cytotoxic immune response. Examples of these adjuvants are the  
20 cytokines of the TH1 response, DNA expression constructs which code for cytokines and immuno-stimulatory DNA sequences.

- To solve the problems described in the introduction, we had recourse to immunisation with DNA. This technique has already been discussed above (see e.g. Ulmer JB et al. (1993), WO91/00539, EP 500799, WO95/19799, US 5,580,859, US 5,589,466  
25 and US 5,593,972).

The vaccine in the invention is intended for the prophylaxis or treatment of infections with lentiviruses, particularly FIV infections in the cat, and is characterised by the

- 7 -

presence of an immunising polynucleotide sequence, which contains or consists of at least a part of the gene of the envelope protein (*env* gene) of the corresponding lentivirus, particularly FIV. This must be under the control of a eukaryotic promoter which is active in the corresponding animal, particularly the cat. "At least a part of the gene of the envelope protein" means that one or more parts of this gene, or the whole gene, are present. The parts of the gene must be large enough to evoke an immune response.

Such a vaccine should preferably contain an immunising polynucleotide sequence for the domain of the *env* gene product which is extracellular or lies outside the virus, as well as a sequence which codes for at least 20 amino acids of the trans-membrane section of the *env* gene product.

Nucleotide sequences which can be used in the present invention and which were used in the context of the embodiments may be found in the separate sequence protocol as SEQ ID NO 1 (FIV gp140), SEQ ID NO 2 (IL-12p40), SEQ ID NO 3 (IL-12p35), SEQ ID NO 4 (IL-16), SEQ ID NO 5 (CpG) and SEQ ID NO 6 (CpG).

The minimal section of the immunising polynucleotide sequence contained in a favoured vaccine may be the sequence given under SEQ ID NO 1, or a sequence which is at least 85% identical to that given under SEQ ID NO 1 or a sequence which is at least 85% identical to that given under SEQ ID NO 1 without degeneration of the genetic code. The similarity of the nucleic acids was calculated with the program MacMolly Complain Version 3.8 ([www.molgen.com](http://www.molgen.com)) and the parameters "gap penalty = 3" and "mismatch penalty = 1".

The sequences given above also include the complementary sequences.

In one embodiment of the invention the vaccine also includes at least one, or better two, accessory polynucleotide sequences. This accessory polynucleotide sequence includes the sequence which codes for IL-12. In particular, for the treatment of *Felidae*, specifically the domestic cat, this should be the sequence which codes for both subunits of feline IL-12, under the control of one or more eukaryotic promoters which are active in the corresponding animal. An additional or alternative possibility is to use the sequence which codes for IL-16. For the treatment of *Felidae*, specifically

- 8 -

the domestic cat, this should be the sequence which codes for feline IL-16. Again this must be under the control of an eukaryotic promoter which is active in the appropriate animal.

5 In a further embodiment of the vaccine, this can contain the sequence which codes for IL-12, for example the sequences which code for the two subunits of feline IL-12, and the sequence which codes for IL-16, for example the sequence which codes for feline IL-16, in the same accessory polynucleotide sequence, under the control of one or more eukaryotic promoters which are active in the appropriate animal, such as the cat.

10 In a further embodiment, the vaccine contains an accessory polynucleotide sequence, which includes the sequence  $N^1N^2CGN^3N^4$  at least once, where  $N^1N^2$  is an element of the group GT, GG, GA, AT or AA and  $N^3N^4$  an element of the group CT or TT. As usual, C stands for cytosine, G for guanine, A for adenine and T for thymine. In the following embodiment, the 5'-phosphorylated oligodesoxynucleotides 5'-  
15 GTTCTTCGGG GCGTTCTTTT TTAAGAACGC CCC (SEQ ID NO 5) and 5'-GAAGAACGTT TTCCAATGAT TTTTCATTGG AAAAC (SEQ ID NO 6), in equimolar quantities and with a total DNA concentration of 1 mg per ml solution, were treated with T4 DNA ligase in the presence of 1 mm ATP. After ligation was complete, unconverted starting material was digested by reaction with T7 DNA polymerase in the absence of dNTPs and purified by anionic exchange HPLC to give the  
20 product.

Preferred sequences to be contained in the vaccine, specifically for the treatment of cats, are sequences in accordance with SEQ ID NO 2 (IL-12), SEQ ID NO 3 (IL-12), SEQ ID NO 4 (IL-16), SEQ ID NO 5 (CpG) or SEQ ID NO 6 (CpG).

25 The polynucleotide sequences or expression constructs, both the immunising and the accessory polynucleotide sequences, may consist of covalently capped linear desoxyribonucleic acid molecules, which include a linear double-stranded region and in which single strands incorporated into double strands are connected by short single-stranded loops of desoxyribonucleic acid nucleotides. These constructs preferably consist of only the coding sequence, under the control of a promoter which is  
30 active in the vaccinated animal and a terminator sequence.

A further object of the present invention is a procedure for the vaccination or treatment of infections with lentiviruses, particularly FIV infections in the cat, which has the particular characteristic that polynucleotide sequences as described above are applied to a suitable carrier, are accelerated, penetrate into the skin cells of the animal, specifically the cat, and are expressed there. A preferred carrier is gold, although other massive inert materials are also suitable.

Aside from the method described above for the use of vaccines with compositions in accordance with the invention, other modes of application can be used, in which the disadvantages mentioned in the discussion of the scientific status are at least partially reduced or preferably absent. These modes of application include, for example, administration of the polynucleotide sequences in aqueous solution by injection into the musculature.

As, according to current theory, the cytotoxic response is important and the development of this response should be provoked by efficient gene expression with as low as possible a contribution from inadvertently expressed proteins, the introduction of the vaccine by ballistic transfer of minimalistic DNA expression constructs is the currently favoured method of administration and is described in the following example.

The aim of the study carried out with ballistic transfer was, if possible, to differentiate the role of the components which make the essential protective contribution to the immune response. It is much more difficult to solve this problem in the cat than, for example, in man or in the mouse. With immunologically well researched species, much can be learnt about the underlying type of response by, for example, typing the antibodies formed in the course of the vaccination (IgG subtype 1 is specific to type 2 immune response, subtype IgG2b is specific to type 1). If the applicability of the type 1 / type 2 paradigm is assumed, this information allows conclusions about the efficacy and direction of a vaccination, even without a study on protection against infection. In this way it is possible to optimise the favoured composition and method of administration to achieve a hypothetically prophylactic immune response with much less effort than if each type of vaccination had to be examined with an experimental test of protection from infection. In the present state of scientific knowledge, it is unfortunately not possible to make such predictions in the cat with the



- 10 -

same degree of confidence as would be the case with species such as the mouse or man. Even fundamental paradigms such as the type 1-type 2 dichotomy have not been demonstrated for the cat. There is a marked concordance between mouse and man in many fundamental immunological characteristics, but in many cases this is restricted to these two species and not transferable to others. This makes the great success of the regimen examined here even more surprising.

Vaccine according to the invention can, instead of polynucleotides, also contain proteins or glycoproteins which are coded by the nucleotide sequences described in the present application, e.g. in Example 1, or similar sequences. A vaccine experiment based on protein was described in detail by Leutenegger et al (1998). In this study a commercial adjuvant (QS-21) was used and the results were unsatisfactory, even though partial protection was achieved in some cats. The activity of vaccines based on proteins can be greatly amplified if protein cytokines (IL-12 and/or IL-16) are used as adjuvants, in accordance with the present invention. Proteins suitable for such vaccines include the proteins of FIV or immunising portions of these and the cytokines IL-12 and IL-16. These can be expressed in bacteria (e.g. *E. coli*), in yeasts, in mammalian cells (e.g. CHO cells), in insect cells (e.g. cells from *Heliothis zea*, ATCC No. CRL-9281), or in plants (e.g. tobacco), and then extracted and purified.

Further advantageous measures are included in the following sub-claims. The invention will now be further explained on the basis of figures and of a concrete embodiment, which should however in no way restrict the invention as defined in the claims.

**Figure 1** shows the results of the quantification of FIV-RNA in cat plasma.

## Embodiments

Five regimens for vaccination were formulated. The basic antigen in all groups, apart from the control group, was the gp140-SU antigen, which is the main product of the FIV *env* gene.

The gene construct mentioned here will be generally referred to as gp140-DNA. The following experiment was planned to test the usefulness of this gene construct. Six groups of 4 cats each were used and these were immunised with different preparations of gp140-DNA and, in some cases, DNA-coded adjuvants, or, in one case, non-coding adjuvant DNA. The DNA constructs were the above mentioned minimalistic expression constructs, consisting solely of a coding sequence preceded by the sequence of the cytomegalovirus promoter (CMV). The coding sequence and the CMV-promotor were used as linear double-stranded molecules, which were covalently capped at both ends to prevent extra- or intracellular degradation from exonucleases. The DNA constructs were adsorbed on small gold particles which were shot directly into the skin of experimental animals. The animals were bombarded with the corresponding constructs three times at intervals of three weeks; the DNA was applied to 1 mg gold per shot. Immunisation was carried out with a Helios gene-gun (Biorad, Munich, D) and a pressure of 500 psi. The total dose of DNA was 2 µg per animal per vaccination. Four weeks after the third vaccination, the animals were subjected to a test infection with the FIV strain which is used to prepare the vaccine antigen (Strain Zurich 2, (Morikawa et al., 1991)). The dose used for the test infection was 25 times the concentration which would cause infection in 50% of cats (cat infective dose 50 = CID<sub>50</sub>). The groups were as follows:

**Table 1** Composition of vaccine groups

Group No.	Vaccine contains:	Issue
1	Only gold particles	Negative controls, no protection expected for these cats
2	gp140-DNA	Efficacy of the gp140-DNA construct alone
3	gp140-DNA + IL-12-DNA	Additional activity of IL-12, in comparison with group 2
4	gp140-DNA + IL-16-DNA	Additional activity of IL-16, in comparison with group 2
5	gp140-DNA + IL-12-DNA + IL-16-DNA	Synergistic activity of IL-12 and IL-16 DNA, in comparison with Groups 3 and 4, respectively
6	gp140-DNA + CpG	Clarification of the effect of CpG,

The protection from the different vaccines was determined by measuring the following parameters at weekly intervals (Exception: The RNA loads were measured only in week 5):

- 5           1. Antibodies to the transmembrane protein (TM) were determined by an ELISA procedure.
2. The plasma load of FIV RNA was determined with a TaqMan®-PCR procedure.
3. The amount of FIV-DNA which is incorporated into lymphocyte DNA, the so-called provirus-DNA, was determined with a TaqMan® procedure (Leutenegger et al. 1999).
- 10

The results can be summarised as follows:

1.       *Seroconversion against TM:* The course of the seroconversion is summarised in Table 2.

15           It can be seen here that the animals in Control Group 1 seroconverted extraordinarily strongly, which suggests that the rate of virus replication is high. From the fifth week, four out of four animals in this group were seropositive.

          In Group 2, seroconversion occurred only gradually and the degree of seroconversion was much lower than in Group 1. Even in the ninth week not all animals in Group 2 were seropositive. This suggests that there is less virus replication, which is compatible with protection.

20

          In Group 3 only one animal seroconverted by the seventh week and the others remained fully negative. This suggests that three of the four animals were completely protected. The seroconversion in the single animal was low in comparison to the animals in Group 1, which suggests that there is only moderate virus replication.

25

- 13 -

In Group 4 two of the four animals seroconverted by the seventh week. Here too, only low levels of antibodies were formed, which also suggests that there are only low levels of virus replication. The combination of IL-12 and IL-16 in Group 5 turned out not to be effective against seroconversion. Four of the four animals had seroconverted by the seventh week.

The same applies to Group 6 as to Group 5. Here too, four of the four animals had seroconverted by the seventh week.

**Table 2** FIV Vaccine Experiment, TM-ELISA Results

Cat	Group	Weeks after Test Infection												
		-7	-5	-3	0	1	2	3	4	5	6	7	8	10
2916	1	0.7	0	0	0	0.3	0.1	0	1.6	70.9	92.2	86.2	85.9	85.9
2932		1.2	0.3	0.2	0	0.8	0.4	0	1.6	59.8	78.6	96.2	65.6	65.6
381		0.6	1.3	0.1	0	0.4	0.2	0	5.3	78	95.3	72.6	89.3	89.3
384		0	1	0.1	0	0.4	0.7	0	10.7	83.8	90.7	78.7	79.4	79.4
2924	2	0	0.3	0	0	0.04	0.8	0.4	1.9	76.4	94.3	88.7	88.3	88.3
2947		0	1	0.5	0	0.4	0.6	0	0	0.4	1.3	0	60.4	60.4
379		0.6	0.9	0.1	0	0	0.4	0	0.4	0.8	16.7	31.6	82.4	82.4
393		0	0.3	0	0	0	0	0	0.8	66.7	85.7	63.6	90	90
2917	3	0	1.2	0.2	0	0	0.2	0	0	0.1	1.1	0	0.9	0.9
2943		0	0.8	0	0	0	0.8	0	0	0	0.9	0	0.8	0.8
377		1	2.4	2.3	0	2.6	0.4	0	1.6	0	2.1	0	0.5	0.5
388		0	0.2	0	0	0.4	0.1	0	0	54.6	86.6	68.8	80.1	80.1
2922	4	0	0.5	0	0	0.5	0	0	0	0	2.6	0	1.1	1.1
2933		0	0.7	0	0	0.3	0.1	0	0	6.7	88.2	86.6	80.4	80.4
382		0.7	1.4	1.4	0	0	0.7	0	1	0.1	1.4	3	64.3	64.3
394		0.2	1	0.4	0	0	0.3	0	0.4	0.05	39.9	45.7	74.6	74.6
2923	5	0	0.2	0	0	0	0.2	0	0.9	2.6	49.4	41.3	74.4	74.4
2959		0.08	0.6	0	0	0	0.3	0	47.5	88.5	97.2	93.4	79.1	79.1
378		0.4	1.9	0.2	3.6	0	0.3	0	2.9	50	99.2	77.4	81.6	81.6
389		0.08	0.2	0	0	0	0.2	0	0.3	38.3	89.4	73.3	97.8	97.8
2925	6	0.08	0.6	0	0.8	0	0.1	0	5	63.1	80	68	79.4	79.4
2936		0.3	1.2	0.2	0	0	0.4	0	0	8.1	61.2	64.2	60.2	60.2
380		1.4	7.4	0.1	0	0	0.4	0	0	1.3	70.3	56.8	71.8	71.8
385		1.6	9.5	1.2	0	0.7	0.2	0	1.3	9.7	108.3	65.4	87.2	87.2

2. *FIV-RNA Virus load in plasma:* The results of the quantification of FIV-RNA in cat plasma are summarised in Figure 1. The comments on the results are as follows:

Group 1: The RNA virus load was highest here.

- 14 -

Group 2: The cats which had been vaccinated with gp140-DNA exhibited a significantly lower RNA virus load than the control animals. This allows the conclusion that the gp140 construct alone is capable of inducing partial protection. The results agree with the serology.

5           Group 3: Adding IL-12 to the gp140-DNA fully protected the cats against blood virus up to the fifth week. These results also agree with the serological observations.

Group 4: The addition of IL-16-DNA also led to impressive protection, as no viruses were detected in plasma up to the fifth week in this group.

10           Group 5: The addition of both IL-12 and IL-16 turned out to be less effective than either IL-12 or IL-16 alone. In the fifth week RNA was detected in the plasma of three out of four animals. However, the quantity was significantly lower than in the control cats in Group 1.

15           Group 6: Using CpG also gave partial protection, although small quantities of FIV-RNA were detected in all animals in the fifth week.

3.       *Quantity of proviral DNA:* The results on the quantification of proviral DNA are summarised for all the cats in Table 3. The comments on the results are as follows:

20           Group 1: As with the serology and the measurements of RNA, the animals in Group 1 are evidently fully susceptible to the test infection.

Group 2: The animals in Group 2 were also provirus-positive without exception; the mean quantity of FIV provirus was only slightly less than that in the control group.

25           Group 3: The quantity of proviral DNA was lowest in this group, just as was found with the serology and with the measurements of RNA. Only one of the four animals was provirus-positive; the other three were not infected at all.

- 15 -

Group 4: IL-16-DNA too led to a lowered provirus load. Even in the sixth week this was significantly lower than in the control animals.

5 Group 5: Astonishingly, the provirus load was very low in animals which had been given a combination of IL-12 and IL-16. This allows the conclusion that IL-12 and IL-16 together provide significant protection against the integration of provirus into host DNA.

10 Group 6: Equally surprisingly, the effect of CpG addition on the quantity of provirus was also extremely marked. Only traces of integrated provirus could be detected in the sixth week. These results are somewhat in contradiction to the findings with the RNA measurements. They could perhaps be explained if the CpGs assist in inhibiting the integration of the virus into host DNA.

**Table 3** *Provirus load in the individual cats*

Vaccine	Cat	Test Infect.	Week1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 8	Week 10
Gold	2916Y	0.00	0.00	0.00	0.00	720.65	2036.35	3250.62	2150.45	617.83
	2932Y	0.00	0.00	0.00	0.00	471.70	736.38	11649.83	490.65	570.69
	0381Y	0.00	0.00	0.00	0.00	1674.35	5853.32	9818.22	1676.30	2080.08
	0384Y	0.00	0.00	0.00	0.00	114.12	796.11	9393.60	9042.02	1570.48
gp140	2924Y	0.00	0.00	0.00	0.00	1867.55	5395.20	6378.60	17906.93	2661.38
	2947Y	0.00	0.00	0.00	0.00	0.00	0.00	8782.45	949.53	711.82
	0379Y	0.00	0.00	0.00	0.00	0.00	0.00	7096.10	34.97	205.24
	0393Y	0.00	0.00	0.00	0.00	344.56	1470.99	6683.63	709.22	2449.24
gp140 IL-12	2917Y	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	2943Y	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	0377Y	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	0388Y	0.00	0.00	0.00	-	4555.94	4644.27	451.29	429.79	263.25
gp140 IL-16	2922Y	0.00	0.00	0.00	0.00	132.90	0.00	0.00	0.00	0.00
	2933Y	0.00	0.00	0.00	0.00	1169.13	-	3495.44	2205.85	1856.62
	0382Y	0.00	0.00	0.00	0.00	0.00	0.00	2754.58	-	1747.65
	0394Y	0.00	0.00	0.00	0.00	0.00	-	1789.69	915.75	923.14
gp140 IL-12 / IL-16	2923Y	0.00	0.00	0.00	0.00	0.00	-	2347.99	-	3134.67
	2959Y	0.00	0.00	0.00	7.24	2493.99	525.81	0.00	581.62	501.54
	0378Y	0.00	0.00	0.00	8.84	352.15	696.76	517.04	0.00	240.05
	0389Y	0.00	0.00	0.00	0.00	-	3963.26	592.80	2307.76	462.34
gp140 CpG	2936Y	0.00	0.00	0.00	0.00	31.33	232.77	333.68	7.98	82.91
	2925Y	0.00	0.00	0.00	0.00	19.12	51.55	101.89	-	-
	0380Y	0.00	0.00	0.00	0.00	94.31	0.00	8.57	8.24	5.49
	0385Y	0.00	0.00	0.00	0.00	0.00	89.10	337.48	96.46	174.80

--: not determined

5 Taken together, the results allow the surprising conclusion that gp140-DNA administered with various additional components induces different degrees of protection. This protective effect is evident in decreased viral replication, which leads to less or to no seroconversion and/or less integration of viral DNA into the DNA of the host cell.

## List of References

- Amiel C, Darcissac E, Truong MJ, Dewulf J, Loyens M, Mouton Y, Capron A, Bahr GM; (1999) Interleukin-16 (IL-16) inhibits human immunodeficiency virus replication in cells from infected subjects, and serum IL-16 levels drop with disease progression. *J Infect Dis*, 179(1):83-91
- 5 Boretti and F. (1999) Experimentelle Immunisierung von Katzen mit rekombinanten Hüllglykoproteinen des Feline Immunschwächevirus: Einfluss verschiedener Impfstoffformulierungen auf die Immunantwort und Vergleich mit einer Ganzvirusvakzine. *Vet.-Diss. Zürich*, .
- 10 Chu, R.S., Targoni, O.S., Krieg, A.M., Lehmann, P.V. and Harding, C.V. (1997) CpG oligodeoxynucleotides act as adjuvants that switch on T helper 1 (Th1) immunity. *Journal of Experimental Medicine* 186(10), 1623-31
- Gardner, M.B. (1991) Simian and feline immunodeficiency viruses: animal lentivirus models for evaluation of AIDS vaccines and antiviral agents. [Review] [82 refs]. *Antiviral Research* 15(4), 267-86.
- 15 Gunzburg WH, Salmons B, (1995) Virus vector design in gene therapy. *Mol Med Today* 1(9):410-7)
- Hofmann-Lehmann, R., Holznagel, E., Aubert, A., Bauer-Pham, K. and Lutz, H. (1995) FIV vaccine studies. II. Clinical findings, hematological changes and kinetics of blood lymphocyte subsets. *Veterinary Immunology & Immunopathology* 46(1-2), 115-25.
- 20 Huisman, W., Karlas, J.A., Siebelink, K.H., Huisman, R.C., de Ronde, A., Francis, M.J., Rimmelzwaan, G.F. and Osterhaus, A.D. (1998) Feline immunodeficiency virus subunit vaccines that induce virus neutralising antibodies but no protection against challenge infection. *Vaccine* 16(2-3), 181-7.
- 25 Idziorek T, Khalife J, Billaut-Mulot O, Hermann E, Aumercier M, Mouton Y, Capron A, Bahr GM (1998) Recombinant human IL-16 inhibits HIV-1 replication and protects against activation-induced cell death (AICD) *Clin Exp Immunol*;112(1):84-91
- Jarrett, O., Yamamoto, J.K. and Neil, J.C. (1990) Feline immunodeficiency virus as a model for AIDS vaccination. [Review] [15 refs]. *Aids* 4(Suppl 1), S163-5.
- 30 Krieg AM, Yi AK, Matson S, Waldschmidt TJ, Bishop GA, Teasdale R, Koretzky GA, Klinman DM (1995) CpG motifs in bacterial DNA trigger direct B-cell activation, *Nature* 374(6522):546-9.
- Leutenegger, C.M., Hofmann-Lehmann, R., Holznagel, E., Cuisinier, A.M., Wolfensberger, C., Duquesne, V., Cronier, J., Allenspach, K., Aubert, A., Ossent, P. and



- Lutz, H. (1998) Partial protection by vaccination with recombinant feline immunodeficiency virus surface glycoproteins. *AIDS Research & Human Retroviruses* 14(3), 275-83.
- 5 Lutz, H., Hofmann-Lehmann, R., Bauer-Pham, K., Holznagel, E., Tozzini, F., Bendinelli, M., Reubel, G., Aubert, A., Davis, D., Cox, D. and et al. (1995) FIV vaccine studies. I. Immune response to recombinant FIV env gene products and outcome after challenge infection. *Veterinary Immunology & Immunopathology* 46(1-2), 103-13.
- 10 Lutz, H., Hofmann-Lehmann, R., Leutenegger, C., Allenspach, K., Cuisinier, A.M., Cronier, J., Duquesne, V. and Aubert, A. (1996) Vaccination of cats with recombinant envelope glycoprotein of feline immunodeficiency virus: decreased viral load after challenge infection. [Review] [17 refs]. *AIDS Research & Human Retroviruses* 12(5), 431-3.
- 15 Lipford, G.B., Bauer, M., Blank, C., Reiter, R., Wagner, H. and Heeg, K. (1997) CpG-containing synthetic oligonucleotides promote B and cytotoxic T cell responses to protein antigen: a new class of vaccine adjuvants. *European Journal of Immunology* 27(9), 2340-4.
- Mackewicz CE, Barker E, Levy JA, (1996) Role of beta-chemokines in suppressing HIV replication. *Science*, 22;274(5291):1393-5
- 20 Morikawa, S., Lutz, H., Aubert, A. and Bishop, D.H. (1991) Identification of conserved and variable regions in the envelope glycoprotein sequences of two feline immunodeficiency viruses isolated in Zurich, Switzerland. *Virus Research* 21(1), 53-63.
- 25 Osterhaus, A.D., Tijhaar, E., Huisman, R.C., Huisman, W., Darby, I.H., Francis, M.J., Rimmelzwaan, G.F. and Siebelink, K.H. (1996) Accelerated viremia in cats vaccinated with recombinant vaccinia virus expressing envelope glycoprotein of feline immunodeficiency virus. *AIDS Research & Human Retroviruses* 12(5), 437-41.
- 30 Pedersen, N.C., Ho, E.W., Brown, M.L. and Yamamoto, J.K. (1987) Isolation of a T-lymphotropic virus from domestic cats with an immunodeficiency-like syndrome. *Science* 235(4790), 790-3.
- Richardson, J., Moraillon, A., Baud, S., Cuisinier, A.M., Sonigo, P. and Pancino, G. (1997) Enhancement of feline immunodeficiency virus (FIV) infection after DNA vaccination with the FIV envelope. *Journal of Virology* 71(12), 9640-9.
- 35 Richardson, J., Moraillon, A., Crespeau, F., Baud, S., Sonigo, P. and Pancino, G. (1998) Delayed infection after immunization with a peptide from the transmembrane glycoprotein of the feline immunodeficiency virus. *Journal of Virology* 72(3), 2406-15.

- Romagnani, S., Maggi, E. and Del Prete, G. (1994) An alternative view of the Th1/Th2 switch hypothesis in HIV infection. *AIDS Research & Human Retroviruses* 10(5), iii-ix.
- 5 Tonelli, Q.J. (1991) Enzyme-linked immunosorbent assay methods for detection of feline leukemia virus and feline immunodeficiency virus. [Review] [7 refs]. *Journal of the American Veterinary Medical Association* 199(10), 1336-9.
- Torten, M., Franchini, M., Barlough, J.E., George, J.W., Mozes, E., Lutz, H. and Pedersen, N.C. (1991) Progressive immune dysfunction in cats experimentally infected with feline immunodeficiency virus. *Journal of Virology* 65(5), 2225-30.
- 10 Ulmer JB, Donnelly JJ, Parker SE, Rhodes GH, Felgner PL, Dwarki VJ, Gromkowski SH, Deck RR, De Witt CM, Friedman A et al. (1993) Heterologous protection against influenza by injection of DNA encoding a viral protein. *Science* 259: 1745-1749).
- 15 Yamamoto, J.K., Hohdatsu, T., Olmsted, R.A., Pu, R., Louie, H., Zochlinski, H.A., Acevedo, V., Johnson, H.M., Soulds, G.A. and Gardner, M.B. (1993) Experimental vaccine protection against homologous and heterologous strains of feline immunodeficiency virus. *Journal of Virology* 67(1), 601-5.
- Yamamoto, J.K., Okuda, T., Ackley, C.D., Louie, H., Pembroke, E., Zochlinski, H., Munn, R.J. and Gardner, M.B. (1991) Experimental vaccine protection against feline immunodeficiency virus. *AIDS Research & Human Retroviruses* 7(11), 911-22.
- 20 Zhou P, Goldstein S, Devadas K, Tewari D, Notkins AL, (1997) Human CD4+ cells transfected with IL-16 cDNA are resistant to HIV-1 infection: inhibition of mRNA expression. *Nat Med* 3(6):659-64.

### Patent Claims

1. Vaccine for the protective vaccination or therapy of a lentivirus infection in *Felidae* which has the characteristic that it contains an immunising polynucleotide sequence which contains or consists of at least a part of the gene of a protein of the corresponding virus, particularly of the envelope protein (*env* gene), under the control of a eukaryotic promoter which is active in the corresponding animal.
2. Vaccine in accordance with Claim 1 which has the characteristic that the lentivirus is a lentivirus of an animal of the genus *Felidae*, specifically the domestic cat.
3. Vaccine in accordance with Claim 2 which has the characteristic that the lentivirus is the feline immune deficiency virus (FIV).
4. Vaccine in accordance with Claims 1 to 3 which has the characteristic that the immunising polynucleotide sequence contains a coding sequence which contains or consists of the extraviral or extracellularly situated domain of the *env* gene product, or a part of this.
5. Vaccine in accordance with Claim 4 which has the characteristic that the immunising polynucleotide sequence contains or consists of a coding sequence for at least twenty aminoacids of the transmembrane portion of the *env* gene product.
6. Vaccine in accordance with Claims 1 to 5 which has the characteristic that it also contains at least one immunising section of the gene coding for an internal protein of the lentivirus, for example the *gag* gene.

- 5 7. Vaccine in accordance with claims 1 to 6 which has the characteristic that the immunising polynucleotide sequence contains the coding sequence (SEQ ID NO. 4) of the plasmid sequence given under SEQ ID NO 1 or a sequence which is 85% identical with the coding sequence (SEQ ID NO 4) of the plasmid sequence given under SEQ ID NO 1, or a coding sequence which, without degeneration of the genetic code, is at least 85% identical with the coding sequence of the sequence given under SEQ ID NO 1.
- 10 8. Vaccine in accordance with Claims 1 to 7 which is characterised by containing an accessory polynucleotide sequence which contains the sequences coding for IL-12 under the control of one or more eukaryotic promoters which are active in the corresponding animal.
- 15 9. Vaccine in accordance with Claims 1 to 7 which is characterised by containing an accessory polynucleotide sequence which contains the sequence coding for IL-16 under the control of a eukaryotic promoter which is active in the corresponding animal.
- 20 10. Vaccine in accordance with Claims 1 to 7 which is characterised by containing an accessory polynucleotide sequence which contains the sequence coding for IL-12 and IL-16 under the control of one or more eukaryotic promoters which are active in the corresponding animal.
- 25 11. Vaccine in accordance with Claims 8 to 10 which is characterised by containing an accessory polynucleotide sequence which codes for both subunits of feline IL-12 and/or for feline IL-16 and that these sequences are under the control of a eukaryotic promoter which is active in the cat.
12. Vaccine in accordance with Claims 8 to 11 which is characterised by containing an accessory polynucleotide sequence which contains at least one base sequence of the type  $N^1N^2CGN^3N^4$ , where  $N^1N^2$  is an element of the group GT, GG, GA, AT or AA and  $N^3N^4$  is an element of the group CT or TT.

13. Vaccine in accordance with at least one of Claims 1 to 12 which is characterised by the fact that the immunising polynucleotide sequences and/or the accessory polynucleotide sequences are present as expression constructs which consist of linear and covalently capped molecules of desoxyribonucleic acid which contain a linear double-stranded region and in which the single strands which combine to form double strands are connected by short single-stranded loops of desoxyribonucleic acid and in which the single strands which combine to form double strands only consist of the coding sequence, a terminator sequence and a promoter which is active in the animal which is immunised.
14. Vaccine in accordance with Claims 8 to 13 which is characterised by the fact that the accessory polynucleotide sequence contains a coding sequence in accordance with SEQ ID NO 8 (IL-12 p40), a coding sequence in accordance with SEQ ID NO 9 (IL-12 p35), coding sequences SEQ ID NO 10 (IL-16), SEQ ID NO 5 (CpG) or SEQ ID NO 6 (CpG) or a sequence which is complementary to one of these sequences.
15. Vaccine in accordance with Claims 1 to 14 for the vaccination or therapy of lentivirus infections in animals characterised by the presence of an immunising polynucleotide sequence and, in some cases, an accessory polynucleotide sequence in accordance with Claims 8 to 12, applied to a suitable massive and inert carrier material, in such a way that it can be accelerated into the skin of the animal, penetrate into the cells of the animal and be expressed there.
16. Vaccine in accordance with Claim 15 which is characterised by the animal belonging to the genus of the Felidae, specifically the domestic cat.
17. Vaccine in accordance with Claims 15 or 16 which is characterised by the carrier material being gold.
18. Vaccine for the protective vaccination or therapy of an infection with lentivirus in *Felidae* which is characterised by the fact that it contains an immunising protein or part of a protein, particularly the envelope protein of

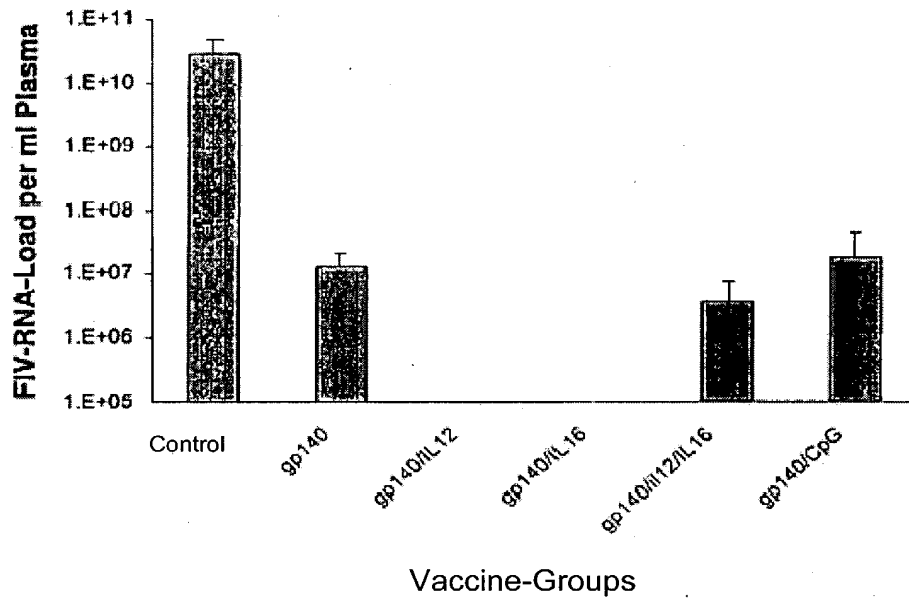
the corresponding lentivirus, together with IL-12 and/or IL-16 in the form of protein.

- 5 19. Procedure for the preparation of an immunising lentivirus protein or immunising parts of this, particularly of proteins or parts of proteins of FIV, which has the characteristic that a corresponding nucleotide sequence is expressed under the control of suitable expression sequences in the host cell and isolated from this.

# **ABSTRACT OF THE DISCLOSURE**

A vaccine is described which is capable of inducing protection to disease consequent to an infection with lentivirus, in particular an infection with the feline immune deficiency virus (FIV), whereby the vaccination can be carried out in such a way that vaccinated animals can be distinguished from infected or diseased animals on the basis of their antibody status. A vaccine of this type includes a DNA sequence which codes for the envelope glycoprotein and preferably also contains a portion of the gene which codes for the transmembrane protein. A further aspect of the invention is that suitable adjuvants are included in the vaccine mixture which induce a cytotoxic immune response, for example cytokines of the TH1 Response, cytokine-coding DNA expression constructs or immuno-stimulatory DNA sequences.

FIV-RNA Load in Week 5





**Declaration and Power of Attorney for Patent Application  
Déclaration et Pouvoirs pour Demande de Brevet  
French Language Declaration**

En tant l'inventeur nommé ci-après, je déclare  
par le présent acte que :

Mon domicile, mon adresse postale et ma  
nationalité sont ceux figurant ci-dessous à côté  
de mon nom.

Je crois être le premier inventeur original et  
unique (si un seul nom est mentionné ci-  
dessous), ou l'un des premiers co-inventeurs  
originaux (si plusieurs noms sont mentionnés  
ci-dessous) de l'objet revendiqué, pour lequel  
une demande de brevet a été déposée  
concernant l'invention intitulée

et dont la description est fournie ci-joint à  
moins

☐ ci-joint

☐ a été déposée le

sous le numéro de demande des  
Etats-Unis ou le numéro de demande  
international PCT

et modifiée le

(le cas échéant).

Je déclare par le présent acte avoir passé en  
revue et compris le contenu de la description  
ci-dessus, revendications comprises, telles que  
modifiées par toute modification dont il aura  
été fait références ci-dessus.

Je reconnais devoir divulguer toute  
information pertinente à la brevetabilité,  
comme défini dans le Titre 37, § 1.56 du Code  
fédéral des réglementations.

As a below named inventor, I hereby declare  
that :

My residence, post office address and  
citizenship are as stated next to my name.

I believe I am the original, first and sole  
inventor (if only one name is listed below) or  
an original, first and joint inventor (if plural  
names are listed below) of the subject matter  
which is claimed an for which a patent is  
sought on the invention entitled

**VACCINE AGAINST LENTIVIRAL  
INFECTIONS, SUCH AS THE FELINE  
IMMUNE DEFICIENCY VIRUS OF THE  
CAT**

the specification of which :

☐ is attached hereto.

☒ was filed on January 8, 2002

as United States Application Number  
10/030,500 or PCT International  
Application Number

and was amended on

(if applicable).

I hereby state that I have reviewed and  
understand the contents of the above identified  
specification, including the claims, as amended  
by any amendment referred to above.

I acknowledge the duty to disclose information  
which is material to patentability as defined in  
Title 37, Code of Federal Regulations, § 1.56.

### French Language Declaration

Je revendique par le présent acte avoir la priorité étrangère, en vertu du Titre 35, § 119(a)-(d) ou § 365(b) du Code des Etats-Unis, sur toute demande étrangère de brevet ou certificat d'inventeur ou, en vertu du Titre 35, § 365(a) du même Code, sur toute demande internationale PCT désignant au moins un pays autre que les Etats-Unis et figurant ci-dessous et, en cochant la case, j'ai aussi indiqué ci-dessous toute demande étrangère de brevet, tout certificat d'inventeur ou toute demande internationale PCT ayant date de dépôt précédant celle de la demande à propos de laquelle une priorité est revendiquée.

Prior Foreign application(s)  
Demande(s) de brevet antérieure(s) dans un autre pays.  
1258/1999 SWITZERLAND

(Number) (Country)  
(Numéro) (Pays)

(Number) (Country)  
(Numéro) (Pays)

Je revendique par le présent acte tout bénéfice, en vertu du Titre 35, § 119(e) du Code des Etats-Unis, de toute demande de brevet provisoire effectuée aux Etats-Unis et figurant ci-dessous.

(Application No.) (Filing Date)  
(N° de demande) (Date de dépôt)

Je revendique par le présent acte tout bénéfice, en vertu du Titre 35, § 120 du Code des Etats-Unis, de toute demande de brevet effectuée aux Etats-Unis, ou en vertu du Titre 35, § 365(c) du même Code, de toute demande internationale PCT désignant les Etats-Unis et figurant ci-dessous et, dans la mesure où l'objet de chacune des revendications de cette demande de brevet n'est pas divulgué dans la demande antérieure américaine ou internationale PCT, en vertu des dispositions du premier paragraphe du Titre 35, § 112 du code des Etats-Unis, je reconnais devoir divulguer toute information pertinente à la brevetabilité, comme défini dans le Titre 37, § 1.56 du Code fédéral des réglementations, dont j'ai pu disposer entre la date de dépôt de la demande antérieure et la date de dépôt de la demande nationale ou internationale PCT de la présente demande :

(Application No.) (Filing Date)  
(N° de demande) (Date de dépôt)

(Application No.) (Filing Date)  
(N° de demande) (Date de dépôt)

Je déclare que par le présent acte que toute déclaration ci-incluse est, à ma connaissance, véridique et que toute déclaration formulée à partir de renseignements ou de suppositions est tenue pour véridique; et de plus, que toutes ces déclarations ont été formulées en sachant que toute fausse déclaration volontaire ou son équivalent est passible d'une amende ou d'une incarcération, ou des deux, en vertu de la section 1001 du Titre 18 du Code de Etats-Unis, et que de telles déclarations volontairement fausses risquent de compromettre la validité de la demande de brevet ou du brevet délivré à partir de celle-ci.

I hereby claim foreign priority under Title 35, United States Code, § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT International application which designated at least one country other than the United States, listed below, and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

Priority claimed  
Droit de priorité  
revendiqué

8 July 1999

(Day/Month/Year Filed)  
(Jour/Mois/Année de dépôt)

☒ ☐  
Yes No  
Oui Non

(Day/Month/Year Filed)  
(Jour/Mois/Année de dépôt)

☐ ☐  
Yes No  
Oui Non

I hereby claim the benefit under Title 35, United States Code, § 119(e) of any United States provisional application(s) listed below.

(Application No.) (Filing Date)  
(N° de demande) (Date de dépôt)

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s), or § 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

(Status) (patented, pending, abandoned)  
(Statut) (breveté, en cours d'examen, abandonné)

(Status) (patented, pending, abandoned)  
(Statut) (breveté, en cours d'examen, abandonné)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

## French Language Declaration

**POUVOIRS :** En tant que l'inventeur cité, je désigne par la présente l'(les) avocat(s) et/ou agent(s) suivant(s) pour qu'ils poursuive(nt) la procédure de cette demande de brevet et traite(nt) toute affaire s'y rapportant avec l'Office des brevets et des marques: (mentionner le nom et le numéro d'enregistrement).

**POWER OF ATTORNEY :** As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to persecute this application and transact all business in the Patent and Trademark Office connected therewith: (list name and registration number)

All practitioners associated with  
CUSTOMER NUMBER 600826

RAYMOND O. LINKER, JR. Registration No. 26,419

Adresser toute correspondance à :

Send Correspondence to :

ALSTON & BIRD LLP  
Bank of America Plaza  
101 South Tryon Street, Suite 4000  
CHARLOTTE, NC 28203-4000 U.S.A.

Adresser tout appel téléphonique à :  
(nom et numéro de téléphone)

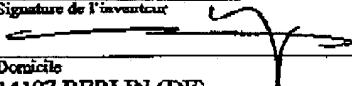
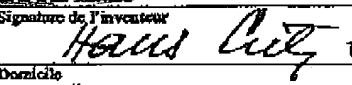
Direct Telephone calls to : (name and telephone number)  
(704) 444-1000

Nom complet de l'unique ou premier inventeur <b>LEUTENEGGER Christian</b>		Full name of sole or first inventor	
Signature de l'inventeur <i>C. Leutenegger</i>	Date 10-5-02	Inventor's signature	Date
Domicile <b>8610 USTER (CH)</b>		Residence	
Nationalité <b>Suisse</b>		Citizenship	
Adresse Postale <b>Höchststrasse 1, CH-8610 USTER (CH)</b>		Post Office Address	
Nom complet du second co-inventeur, le cas échéant <b>SCHROFF Matthias</b>		Full name of second joint inventor, if any	
Signature de l'inventeur <i>M. Schrott</i>	Date	Second inventor's signature	Date
Domicile <b>14057 BERLIN (DE)</b>		Residence	
Nationalité <b>Allemande</b>		Citizenship	
Adresse Postale <b>Friedbergstrasse 5, D-14057 BERLIN (DE)</b>		Post Office Address	

(Fournir les mêmes renseignements et la signature de tout co-inventeur supplémentaire.)

(Supply similar information and signature for third and subsequent joint inventors.)

## French Language Declaration

Nom complet du troisième co-inventeur, le cas échéant <b>WITTIG Burghardt</b>		Full name of third joint inventor, if any	
Signature de l'inventeur 	Date	Third inventor's signature	Date
Domicile <b>14197 BERLIN (DE)</b>		Residence <b>DEX</b>	
Nationalité <b>Allemande</b>		Citizenship	
Adresse Postale <b>Offenbacher Strasse 5, D-14197 BERLIN (DE)</b>		Post Office Address	
Nom complet du quatrième co-inventeur, le cas échéant <b>LUTZ Hans</b>		Full name of fourth joint inventor, if any	
Signature de l'inventeur 	Date <b>10-5-02</b>	Fourth inventor's signature	Date
Domicile <b>8455 RÜDLINGEN (CH)</b>		Residence <b>CHX</b>	
Nationalité <b>Suisse</b>		Citizenship	
Adresse Postale <b>Im Oberdorf, CH-8455 RÜDLINGEN (CH)</b>		Post Office Address	
Nom complet du cinquième co-inventeur, le cas échéant		Full name of fifth joint inventor, if any	
Signature de l'inventeur	Date	Fifth inventor's signature	Date
Domicile		Residence	
Nationalité		Citizenship	
Adresse Postale		Post Office Address	
Nom complet du sixième co-inventeur, le cas échéant		Full name of sixth joint inventor, if any	
Signature de l'inventeur	Date	Sixth inventor's signature	Date
Domicile		Residence	
Nationalité		Citizenship	
Adresse Postale		Post Office Address	

(Fournir les mêmes renseignements et la signature de tout co-inventeur supplémentaire.)

Supply similar information and signature for third and subsequent joint inventors.)